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FILE 'HOME' ENTERED AT 12:29:05 ON 11 APR 2006

=> s (angiotensin converting enzyme or ACE) and crystal and x-ray
L1          26 FILE MEDLINE
L2          47 FILE CAPLUS
L3          55 FILE SCISEARCH
L4           2 FILE LIFESCI
L5          25 FILE BIOSIS
L6          22 FILE EMBASE

TOTAL FOR ALL FILES
L7         177 (ANGIOTENSIN CONVERTING ENZYME OR ACE) AND CRYSTAL AND X-RAY

=> s l7 not 2003-2006/py

TOTAL FOR ALL FILES
L14        105 L7 NOT 2003-2006/PY

=> dup rem l14
PROCESSING COMPLETED FOR L14
L15         65 DUP REM L14 (40 DUPLICATES REMOVED)

=> d ibib abs 1-65

L15  ANSWER 1 OF 65  CAPLUS  COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER:        2002:808426  CAPLUS Full-text
DOCUMENT NUMBER:         137:316076
TITLE:                   Preparation of lisinopril monohydrate
INVENTOR(S):             Brown, John
PATENT ASSIGNEE(S):      Astrazeneca AB, Swed.
SOURCE:                  U.S., 11 pp.
                         CODEN: USXXAM
DOCUMENT TYPE:           Patent
LANGUAGE:                English
FAMILY ACC. NUM. COUNT:  1
PATENT INFORMATION:

     PATENT NO.          KIND   DATE        APPLICATION NO.        DATE
     --------------      ----   --------    -------------------    --------
     US 6468976           B1    20021022    US 2001-950472         20010910
PRIORITY APPLN. INFO.:                      US 2001-950472         20010910
AB     The present invention relates to a novel monohydrate form of 1-(N2-[(S)-1-carboxy-3-
       phenylpropyl]-L-lysyl)-L-proline known under the generic name lisinopril. Further, the
       present invention also relates to the use of the novel monohydrate form of lisinopril for
       the treatment of hypertension and other cardiovascular diseases, pharmaceutical compns.
       containing it as well as processes for the preparation of the monohydrate form of
       lisinopril. Crystalline lisinopril dihydrate was dissolved in 250 mL MeOH in a suitable
       vessel and heated briefly to reflux (60-65°). The solution was then filtered to remove
       any undissolved lisinopril and left to crystallize through self-cooling. The crystals
       formed were then isolated by filtration. The crystalline lisinopril dihydrate was
       dissolved in 50 mL water and then heated to about 45° until the volume of solvent (water)
       was reduced to about 10 mL. Isobutanol was then added and the resulting mixture was
       stirred overnight. The crystals formed were isolated by filtration and dried at 80° for 2
       days. The monohydrate was characterized by x-ray diffraction and spectral methods.
REFERENCE COUNT:         12    THERE ARE 12 CITED REFERENCES AVAILABLE FOR THIS
                               RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15  ANSWER 2 OF 65  SCISEARCH  COPYRIGHT (c) 2006 The Thomson Corporation  on
     STN
ACCESSION NUMBER:    2002:951713  SCISEARCH Full-text
THE GENUINE ARTICLE: 617DC
TITLE:               Sulfamide-based inhibitors for carboxypeptidase A. Novel
                     type transition state analogue inhibitors for zinc
                     proteases
AUTHOR:              Park J D; Kim D H (Reprint); Kim S J; Woo J R; Ryu S E
CORPORATE SOURCE:    Pohang Univ Sci & Technol, Ctr Integrated Mol Syst, Div
                     Mol & Life Sci, Nam Ku, San 31 Hyoja Dong, Pohang 790784,
                     South Korea (Reprint); Pohang Univ Sci & Technol, Ctr
                     Integrated Mol Syst, Div Mol & Life Sci, Nam Ku, Pohang
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790784, South Korea; Korea Res Inst Biosci & Biotechnol, Ctr Cellular Switch Prot Struct, Yusong Gu, Taejon 305806, South Korea

COUNTRY OF AUTHOR: South Korea

SOURCE: JOURNAL OF MEDICINAL CHEMISTRY, (21 NOV 2002) Vol. 45, No. 24, pp. 5295-5302.
ISSN: 0022-2623.

PUBLISHER: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036 USA.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 63

ENTRY DATE: Entered STN: 13 Dec 2002
Last Updated on STN: 13 Dec 2002

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB N-Sulfamoylphenylalanine and its derivatives having varied alkyl groups on the terminal amino group were designed rationally as transition state analogue inhibitors for carboxypeptidase A (CPA) and synthesized. In CPA inhibitory assays the parent compound having the (S)configuration, i.e., (S)-1a, showed potent inhibitory activity with the K-i value of 0.64 muM. Its enantiomer was shown to be much less potent (K-i = 470 muM). Introduction of an alkyl group such as methyl or isopropyl group on the terminal amino group of (S)-1a lowered the inhibitory potency drastically. Introduction of a methyl group on the internal amino group of (S)-1a also caused a drastic reduction of the inhibitory activity. The structure of the CPA-(S)-1a complex determined by single-crystal X- ray diffraction reveals that the sulfamoyl moiety interacts with the zinc ion and functional groups at the active site of CPA, which is reminiscent of the postulated stabilization mode of a tetrahedral transition state in the CPA-catalyzed hydrolysis of a peptide substrate. On the basis of the design rationale and the binding mode of (S)-1a to CPA shown by X-ray crystallographic analysis, the present inhibitors are inferred to be a novel type of transition state analogue inhibitor for CPA.

L15 ANSWER 3 OF 65 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:887772 SCISEARCH Full-text

THE GENUINE ARTICLE: 608YU

TITLE: Syntheses, crystal structures and reactivity of organometallic tantalum(IV) phosphinidene complexes: trans-[{Cp]TaCl(mu-PR)}(2)] (Cp] = C5Me5, R = Cy, tBu, Ph), cis- and trans-[{Cp]TaCl(mu-PMes)}(2)] (Mes=2,4,6-Me3C6H2) and cis-[{Cp ' TaCl(mu-PMes)}(2)] (Cp ' = C5H4Me)

AUTHOR: Blaurock S; Hey-Hawkins E (Reprint)

CORPORATE SOURCE: Univ Leipzig, Inst Anorgan Chem, Johannisallee 29, D-04103 Leipzig, Germany (Reprint); Univ Leipzig, Inst Anorgan Chem, D-04103 Leipzig, Germany

COUNTRY OF AUTHOR: Germany

SOURCE: EUROPEAN JOURNAL OF INORGANIC CHEMISTRY, (NOV 2002) No. 11, pp. 2975-2984.
ISSN: 1434-1948.

PUBLISHER: WILEY-V C H VERLAG GMBH, PO BOX 10 11 61, D-69451 WEINHEIM, GERMANY.

DOCUMENT TYPE: Article; Journal

LANGUAGE: English

REFERENCE COUNT: 84

ENTRY DATE: Entered STN: 22 Nov 2002
Last Updated on STN: 22 Nov 2002

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The reaction of [Cp.TaCl4] (CP. = C5Me5) with LiPHR (1: 1 or 1:2) gives the phosphinidene-bridged tantalum(IV) complexes trans-[{Cp.TaCl(mu-PR)}(2)] [R = Cy (1), tBu (2), Ph (3), 2,4,6-Me3C6H2 (Mes) (4b)]. When the reaction with LiPHMes is carried out in a 1:1 ratio, cis-[{Cp.TaCl(mu-PMes)}(2)] (4a) is also formed besides 4b. For comparison, cis-[JCp'TaCl(mu-PMes))21 (5) was prepared from [Cp'TaCl4] (CP' = C5MeH4) and LiPHMes (1: 1). 1-5 are diamagnetic and were characterised spectroscopically (IR, MS; H-1, P-31, C-13 NMR). Crystal structure determinations on 1-5 showed the presence of dimeric phosphinidene-bridged Ta-IV complexes. The phosphinidene-bridged complexes 1, 3 and 4b do not react with ace-tone, benzophenone, acetonitrile, CS2 (1, 3), acetaldehyde (4b), or ethylaluminum dichloride (3). 3 reacts with moist acetone in the presence of traces of air to give the trinuclear cluster [{Cp.TaCl(mu(2)-O)}(3)(mu(3)-O)(mu(2)-O2PHPh)] (6) in

very low yield. With an excess of CyNC, 3 gives [Cp.TaCl(CNCy)(4)]Cl (7), which was characterised by H-1 and C-13 NMR spectroscopy and by crystal structure determination. As a minor product, [(Cp.TaCl2)(2)(mu(2)-O) (eta(2), mu(2)-P2Cy2)] (8) was also obtained in the reaction of [Cp.TaCl4] with LiPHCy. 6 and 8 were only characterised by crystal structure determination. ((C) Wiley-VCH Verlag GmbH, 69451 Weinheim, Germany, 2002).

L15 ANSWER 4 OF 65 MEDLINE on STN
ACCESSION NUMBER: 2002617470 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 12207002
TITLE: Crystal structures of leukotriene A4 hydrolase in complex with captopril and two competitive tight-binding inhibitors.
AUTHOR: Thunnissen Marjolein M G M; Andersson Bjorn; Samuelsson Bengt; Wong Chi-Huey; Haeggstrom Jesper Z
CORPORATE SOURCE: Department of Biochemistry, University of Stockholm, Arrhenius Laboratories A4, S-106 91 Stockholm, Sweden.
SOURCE: The FASEB journal : official publication of the Federation of American Societies for Experimental Biology, (2002 Oct) Vol. 16, No. 12, pp. 1648-50. Electronic Publication: 2002-08-07.
Journal code: 8804484. E-ISSN: 1530-6860.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200212
ENTRY DATE: Entered STN: 20021011
Last Updated on STN: 20030105
Entered Medline: 20021217

AB Leukotriene (LT) A4 hydrolase/aminopeptidase is a bifunctional zinc enzyme that catalyzes the final step in the biosynthesis of LTB4, a potent chemoattractant and immune modulating lipid mediator. Here, we report a high-resolution crystal structure of LTA4 hydrolase in complex with captopril, a classical inhibitor of the zinc peptidase angiotensin-converting enzyme. Captopril makes few interactions with the protein, but its free thiol group is bound to the zinc, apparently accounting for most of its inhibitory action on LTA4 hydrolase. In addition, we have determined the structures of LTA4 hydrolase in complex with two selective tight-binding inhibitors, a thioamine and a hydroxamic acid. Their common benzyloxyphenyl tail, designed to mimic the carbon backbone of LTA4, binds into a narrow hydrophobic cavity in the protein. The free hydroxyl group of the hydroxamic acid makes a suboptimal, monodentate complex with the zinc, and strategies for improved inhibitor design can be deduced from the structure. Taken together, the three crystal structures provide the molecular basis for the divergent pharmacological profiles of LTA4 hydrolase inhibitors. Moreover, they help define the binding pocket for the fatty acid-derived epoxide LTA4 as well as the subsites for a tripeptide substrate, which in turn have important implications for the molecular mechanisms of enzyme catalyses.

L15 ANSWER 5 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2004:28687 CAPLUS Full-text
DOCUMENT NUMBER: 140:387693
TITLE: Synthesis and solution structure of the two peptides that represent the active-zinc containing-sites of Angiotensin Converting Enzyme (ACE)
AUTHOR(S): Galanis, Athanassios S.; Tzakos, Andreas G.; Spyroulias, Georgios A.; Troganis, Anastassios N.; Pairas, Goerge; Manessi-Zoupa, Evy; Gerothanassis, Ioannis P.; Cordopatis, Paul
CORPORATE SOURCE: Department of Pharmacy, University of Patras, Patras, GR-26504, Greece
SOURCE: Peptides 2002, Proceedings of the European Peptide Symposium, 27th, Sorrento, Italy, Aug. 31-Sept. 6, 2002 (2002), 802-803. Editor(s): Benedetti, Ettore; Pedone, Carlo. Edizioni Ziino: Castellammare di Stabia, Italy.
CODEN: 69EYXG; ISBN: 88-900948-1-8
DOCUMENT TYPE: Conference
LANGUAGE: English

AB Two 36-peptides that represent the two catalytic centers of angiotensin converting enzyme (ACE) somatic isoform (ACEN-36 and ACEC-36 that correspond to H361-A396 and H959-A994 regions of ACE somatic isoform, resp.) were synthesized to obtain valuable insights for the structure of peptides through 1H NMR spectroscopy. Three-dimensional homol. models were generated using as template Thermolysin's X-ray structure in attempt to extract further structural information of the two ACE active sites. The two motifs HEMGH and EAIGD comprise the well-known gluzincins' zinc-binding motifs which are always found in all 3D crystal structures in helix conformation, the so-called "two active-site helixes". The NMR solution structure of the free ACEN-36 peptide, the 3D homol. ACE-Zn models and the TLN active site structure exhibit striking similarities.

REFERENCE COUNT: 5 THERE ARE 5 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 6 OF 65 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2002268553 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 12007598
TITLE: Crystallization and preliminary X-ray crystallographic analysis of Ace: a collagen-binding MSCRAMM from Enterococcus faecalis.
AUTHOR: Ponnuraj Karthe; Xu Yi; Moore Dwight; Deivanayagam Champion C S; Boque Lluis; Hook Magnus; Narayana Sthanam V L
CORPORATE SOURCE: School of Optometry and Center for Biophysical Sciences and Engineering, University of Alabama at Birmingham, 1025 18th Street South, Birmingham, AL 35294-0005, USA.
SOURCE: Biochimica et biophysica acta, (2002 Apr 29) Vol. 1596, No. 2, pp. 173-6.
Journal code: 0217513. ISSN: 0006-3002.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200207
ENTRY DATE: Entered STN: 20020515
Last Updated on STN: 20020713
Entered Medline: 20020712

AB Ace is a collagen-binding bacterial cell surface adhesin from Enterococcus faecalis. The collagen-binding domain of Ace (termed Ace40) and its truncated form Ace19 have been crystallized by the vapor-diffusion hanging-drop method. Ace19 was crystallized in two different crystal forms. A complete 1.65 A data set has been collected on the orthorhombic crystal form with unit cell parameters a=38.43 b=48.91 and c=83.73 A. Ace40 was crystallized in the trigonal space group P3(1)21 or P3(2)21 with unit cell parameters a=b=80.24, c=105.91 A; alpha=beta=90 and gamma=120 degrees. A full set of X-ray diffraction data was collected to 2.5 A. Three heavy atom derivative data sets have been successfully obtained for Ace19 crystals and structural analysis is in progress.

L15 ANSWER 7 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 2002:117046 CAPLUS Full-text
DOCUMENT NUMBER: 137:63504
TITLE: The formation and polymerization behavior of Ni(II) α-diimine complexes using various aluminum activators
AUTHOR(S): Maldanis, Richard J.; Wood, John S.; Chandrasekaran, A.; Rausch, Marvin D.; Chien, James C. W.
CORPORATE SOURCE: Department of Chemistry, University of Massachusetts, Lederle Graduate Research Center, Amherst, MA, 01003-4510, USA
SOURCE: Journal of Organometallic Chemistry (2002), 645(1-2), 158-167
CODEN: JORCAI; ISSN: 0022-328X
PUBLISHER: Elsevier Science B.V.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Several Ni(II) α-diimine complexes have been synthesized and examined for ethylene and propylene polymerization in combination with different aluminum co-catalysts. The pre-catalysts used in the study were [ArN:C(Nap)-C(Nap):NAr]NiBr2 (Nap=1,8-naphthdiyl) (1, Ar=2,4,6-trimethyl phenyl; 2, Ar=2-tBu phenyl; 3, Ar=2-iPr phenyl). These complexes were synthesized via a one-pot reaction where the ligand is formed via an acid catalyzed condensation followed by direct addition of nickel(II) bromide. The complexes were also prepared by a two-step procedure where the ligand was first formed by condensation between the appropriate aniline and ace-naphthoquinone, and the resulting ligand was then allowed

to react with (1,2-dimethoxyethane) nickel(II) dibromide. X- ray structural studies of complexes 1 and 2 have been carried out. Di-Et aluminum chloride (DEAC), and 1,3-dichloro-1,3-diisobutyl- dialuminoxane show higher activities for ethylene and propylene polymns. in combination with these Ni(II) α-diimine complexes than does polymethyl aluminoxane (MAO). The mol. weight of the resulting polymers as well as their resp. polydispersity and Tms are also presented. The polypropylene obtained with 1/DEAC and 2/DEAC at 0 °C show similar rr triad percentage as previously reported for polypropylene generated by MAO activated Ni(II) α-diimine complexes.

REFERENCE COUNT: 37 THERE ARE 37 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 8 OF 65 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:379389 SCISEARCH Full-text
THE GENUINE ARTICLE: 543GR
TITLE: Mechanism of action of zinc proteinases: A MNDO/d/H study of alternative general-acid general-base catalytic pathways for carboxypeptidase-A
AUTHOR: Kilshtain-Vardi A; Shoham G; Goldblum A (Reprint)
CORPORATE SOURCE: Hebrew Univ Jerusalem, Sch Pharm, Dept Med Chem, IL-91120 Jerusalem, Israel (Reprint); Hebrew Univ Jerusalem, Sch Pharm, David R Bloom Ctr Pharm, IL-91120 Jerusalem, Israel; Hebrew Univ Jerusalem, Inst Chem, Dept Inorgan & Analyt Chem, IL-91120 Jerusalem, Israel
COUNTRY OF AUTHOR: Israel
SOURCE: INTERNATIONAL JOURNAL OF QUANTUM CHEMISTRY, (5 MAY 2002) Vol. 88, No. 1, pp. 87-98.
ISSN: 0020-7608.
PUBLISHER: JOHN WILEY & SONS INC, 111 RIVER ST, HOBOKEN, NJ 07030 USA
.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 47
ENTRY DATE: Entered STN: 17 May 2002
Last Updated on STN: 17 May 2002
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Two alternative pathways for peptide cleavage by water, both of the general-acid general-base type, have been followed by semiempirical theoretical calculations on a model of the active site. The system of 120 atoms has been carved out of high resolution X-ray coordinates of a carboxypeptidase A (CPA) complex with a ketomethylene inhibitor, pyroglutamic-N-Phe-(CH2CO)-Phe-OH. The method employed was a combination of MNDO/d and MNDO/H which, together, enable one to deal with the effect of zinc and of multiple hydrogen bond interactions, respectively. The first step in both pathways is nucleophilic attack by a hydroxide on the peptide carbonyl, and the second is proton transfer to the nitrogen of the peptide. This second step presents the highest energy barrier for the reaction. Peptide bond cleavage is spontaneous subsequent to proton transfer. The two alternative paths differ little in barrier heights, but the thermodynamic enthalpy difference for the path of one mechanism is some 20 kcal/mol more stable than for the other, The first mechanism is the one proposed by Lipscomb (Acc Chem Res 1989, 22, 62-69) and the second, less stabilizing mechanism was proposed by Mock (J Biol Chem 1991, 266, 6369-6400). Under kinetic control, both reactions are feasible, and new experiments should be designed in order to clarify if only one of the two is operating under most of the relevant conditions. (C) 2002 Wiley Periodicals, Inc.

L15 ANSWER 9 OF 65 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2002:810329 SCISEARCH Full-text
THE GENUINE ARTICLE: 599LJ
TITLE: The aminopeptidase from Aeromonas proteolytica: structure and mechanism of co-catalytic metal centers involved in peptide hydrolysis
AUTHOR: Holz R C (Reprint)
CORPORATE SOURCE: Utah State Univ, Dept Chem & Biochem, Logan, UT 84322 USA (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: COORDINATION CHEMISTRY REVIEWS, (OCT 2002) Vol. 232, No. 1-2, pp. 5-26.
ISSN: 0010-8545.
PUBLISHER: ELSEVIER SCIENCE SA, PO BOX 564, 1001 LAUSANNE,

SWITZERLAND.
DOCUMENT TYPE: General Review; Journal
LANGUAGE: English
REFERENCE COUNT: 125
ENTRY DATE: Entered STN: 25 Oct 2002
Last Updated on STN: 25 Oct 2002
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Enzymes containing multi-metal active sites are central to numerous biological processes and, consequently, characterization of their structure and function is a problem of outstanding importance. One of the least-explored groups of enzymes is the hydrolases that contain dinuclear metal centers. These enzymes play key roles in carcinogenesis, tissue repair, and protein degradation processes. In addition, some of these enzymes can catalyze the hydrolysis of phosphorus(V) compounds found in nerve gases and agricultural neurotoxins. The determination of detailed reaction mechanisms for these enzymes is required for the design of highly potent, specific inhibitors that can function as potential pharmaceuticals. Hydrolytic enzymes that contain dinuclear centers can use every first row divalent transition metal ion from manganese to zinc, except copper. In order to understand the role of each metal ion in catalysis and the apparent non-selectivity of these enzymes towards divalent transition metal ions, it is critical that the reaction mechanism of a prototypical system be determined. The aminopeptidase from Aeromonas proteolytica (AAP) is one of the best mechanistically characterized hydrolytic enzymes that contains a dinuclear center and is, therefore, the focus of this review.

L15 ANSWER 10 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2001:674624 CAPLUS Full-text
DOCUMENT NUMBER: 136:6325
TITLE: Asymmetric synthesis of BB-3497-A potent peptide deformylase inhibitor
AUTHOR(S): Pratt, L. M.; Beckett, R. P.; Davies, S. J.; Launchbury, S. B.; Miller, A.; Spavold, Z. M.; Todd, R. S.; Whittaker, M.
CORPORATE SOURCE: British Biotech Pharmaceuticals Limited, Cowley, Oxford, OX4 6LY, UK
SOURCE: Bioorganic & Medicinal Chemistry Letters (2001), 11(19), 2585-2588
CODEN: BMCLE8; ISSN: 0960-894X
PUBLISHER: Elsevier Science Ltd.
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 136:6325

AB By screening a library of metalloenzyme inhibitors, the N-formyl-hydroxylamine derivative BB-3497 was identified as a potent inhibitor of Escherichia coli peptide deformylase with antibacterial activity both in vitro and in vivo. The homochiral synthesis of BB-3497, involving a novel asym. Michael addition reaction is described.
REFERENCE COUNT: 18 THERE ARE 18 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 11 OF 65 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:51415 SCISEARCH Full-text
THE GENUINE ARTICLE: 509FF
TITLE: Characterization of the solubility and dissolution properties of several new rifampicin polymorphs, solvates, and hydrates
AUTHOR: Henwood S Q (Reprint); Liebenberg W; Tiedt L R; Lotter A P; de Villiers M M
CORPORATE SOURCE: Univ Louisiana, Coll Pharm, Dept Basic Pharmaceut Sci, 700 Univ Ave, Monroe, LA 71209 USA (Reprint); Univ Louisiana, Coll Pharm, Dept Basic Pharmaceut Sci, Monroe, LA 71209 USA; Potchefstroom Univ Christian Higher Educ, Res Inst Ind Pharm, ZA-2520 Potchefstroom, South Africa; Potchefstroom Univ Christian Higher Educ, Lab Microscopy, ZA-2520 Potchefstroom, South Africa
COUNTRY OF AUTHOR: USA; South Africa
SOURCE: DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, (2001) Vol. 27, No. 10, pp. 1017-1030.
ISSN: 0363-9045.
PUBLISHER: MARCEL DEKKER INC, 270 MADISON AVE, NEW YORK, NY 10016 USA

DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 20
ENTRY DATE: Entered STN: 25 Jan 2002
Last Updated on STN: 25 Jan 2002
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Based on reports that tuberculosis is on the increase, this investigation into the physicochemical properties of rifampicin when recrystallized from various solvent systems was undertaken. Rifampicin is an essential component of the currently recommended regimen for treating tuberculosis, although relatively little is known about its solubility and dissolution behavior in relation to its solid-state properties. A rifampicin monohydrate, a rifampicin dihydrate, two amorphous forms, a 1:1 rifampicin: ace tone solvate, and a 1:2 rifampicin:2-pyrrolidone solvate were isolated and characterized using spectral, thermal, and solubility Measurements. The crystal forms were relatively unstable because except for the 2-pyrrolidone solvate, all the hydrated or solvated materials changed to amorphous forms after desolvation. Fourier transform infrared (FTIR) analysis confirmed the favorable three-dimensional organization of the pharmacophore to ensure antibacterial activity, in all the crystal forms except the 2-pyrrolidone solvate. In the 2-pyrrolidone solvate, the strong IR signals of 2-pyrrolidone interfered with the vibrations of the ansa group. The 2-pyrrolidone solvate was the most soluble in phosphate buffer at pH 7.4. This solvate also had the highest solubility (1.58 mg/ml) and the fastest dissolution in water. In 0.1 M HCl, the dihydrate dissolved the quickest. A X-ray amorphous form (amorph II) was the least soluble and had the slowest dissolution rate because the powder was poorly wettable and very electrostatic.

L15 ANSWER 12 OF 65 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2001:474672 SCISEARCH Full-text
THE GENUINE ARTICLE: 441WN
TITLE: Chemical reactivity in solid-state pharmaceuticals: formulation implications
AUTHOR: Byrn S R (Reprint); Xu W; Newman A W
CORPORATE SOURCE: Purdue Univ, W Lafayette, IN 47907 USA (Reprint); Merck & Co Inc, W Point, PA USA; SSCI Inc, W Lafayette, IN 47906 USA
COUNTRY OF AUTHOR: USA
SOURCE: ADVANCED DRUG DELIVERY REVIEWS, (16 MAY 2001) Vol. 48, No. 1, pp. 115-136.
ISSN: 0169-409X.
PUBLISHER: ELSEVIER SCIENCE BV, PO BOX 211, 1000 AE AMSTERDAM, NETHERLANDS.
DOCUMENT TYPE: General Review; Journal
LANGUAGE: English
REFERENCE COUNT: 46
ENTRY DATE: Entered STN: 29 Jun 2001
Last Updated on STN: 29 Jun 2001
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Solid-state reactions that occur in drug substances and formulations include solid-state phase transformations, dehydration/desolvation, and chemical reactions. Chemical reactivity is the focus of this chapter. Of particular interest are cases where the drug-substance may be unstable or react with excipients in the formulation. Water absorption can enhance molecular mobility of solids and lead to solid-state reactivity. Mobility can be measured using various methods including glass transition (T-g) measurements, solid-state NMR, and X-ray crystallography. Solid-state reactions of drug substances can include oxidation. cyclization. hydrolysis, and deamidation. Oxidation studies of vitamin A, peptides (DL-Ala-DL-Met, N-formyl-Met-Leu-Phe methyl ester, and Met-enkaphalin acetate salt), and steroids (hydrocortisone and prednisolone derivatives) are discussed. Cyclization reactions of crystalline and amorphous angiotensin-converting enzyme (ACE) inhibitors (spirapril hydrochloride, quinapril hydrochloride, and moexipril) are presented which investigate mobility and chemical reactivity. Examples of drug-excipient interactions, such as transacylation, the Maillard browning reaction, and acid base reactions are discussed for a variety of compounds including aspirin, fluoxitine, and ibuprofen. Once solid-state reactions are understood in a pharmaceutical system, the necessary steps can be taken to prevent reactivity and improve the stability of drug substances and products.

L15 ANSWER 13 OF 65 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 2000110782 EMBASE Full-text
TITLE: Large variations in one-bond 13C(α)13C(β) J couplings in polypeptides correlate with backbone conformation.
AUTHOR: Cornilescu G.; Bax A.; Case D.A.
CORPORATE SOURCE: A. Bax, Laboratory of Chemical Physics, National Institute of Diabetes, National Institutes of Health, Bethesda, MD 20892, United States
SOURCE: Journal of the American Chemical Society, (15 Mar 2000) Vol. 122, No. 10, pp. 2168-2171. .
ISSN: 0002-7863 CODEN: JACSAT
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 13 Apr 2000
Last Updated on STN: 13 Apr 2000

AB One-bond 1J(CαCβ) scalar couplings, measured in the protein ubiquitin, exhibit a strong dependence on the local backbone conformation. Empirically, the deviation from the 1J(CαCβ) value measured in the corresponding free amino acid, can be expressed as $\Delta 1J(C\alpha C\beta) = 1.3 + 0.6\cos(\psi - 61°) + 2.2\cos[2(\psi - 61°)] - 0.9\cos[2(\phi + 20°)] \pm 0.5$ Hz, where ϕ and ψ are the intraresidue polypeptide backbone torsion angles obtained from ubiquitin's X-ray structure. The relation between 1J(CαCβ) and backbone torsion angles is confirmed by density functional theory (DFT) calculations on the peptide analogue Ace-Ala-NMe.

L15 ANSWER 14 OF 65 MEDLINE on STN

ACCESSION NUMBER: 2001082939 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 11015691
TITLE: Structural characterization of three crystalline modifications of telmisartan by single crystal and high-resolution X-ray powder diffraction.
AUTHOR: Dinnebier R E; Sieger P; Nar H; Shankland K; David W I
CORPORATE SOURCE: Laboratory of Crystallography, University of Bayreuth, D-95440, Bayreuth, Germany.. robert.dinnebier@unibayreuth.de
SOURCE: Journal of pharmaceutical sciences, (2000 Nov) Vol. 89, No. 11, pp. 1465-79.
Journal code: 2985195R. ISSN: 0022-3549.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200101
ENTRY DATE: Entered STN: 20010322
Last Updated on STN: 20010322
Entered Medline: 20010105

AB Three crystalline modifications (A, B, and C) of 4'-[[2-n-propyl-4-methyl- 6-(1-methyl-benzimidazol-2-yl)benzi midazol-1-yl]methyl]biphenyl-2- carboxylic acid (INN name, telmisartan) have been detected and their crystal structures have been determined by single-crystal X-ray diffraction (pseudopolymorph C) and the method of simulated annealing from high-resolution X-ray powder diffraction data (polymorphs A and B). The compound is of interest because of its use as an angiotensin II receptor antagonist. Polymorph A crystallizes in space group P2(I)/c, Z = 4, with unit cell parameters a = 18.7798(3), b = 18.1043(2), and c = 8.00578(7) A, beta = 97.066(1) degrees, and V = 2701.31 A(3). Polymorph B crystallizes in space group P2(I)/a, Z = 4, with unit cell parameters a = 16.0646(5), b = 13.0909(3), and c = 13.3231(3) A, beta = 99.402(1) degrees, and V = 2764.2(1) A(3). The solvated form C crystallizes in space group C2/c, Z = 8, with unit cell parameters a = 30.990(5), b = 13.130(3), and c = 16.381(3) A, beta = 95.02(2) degrees, and V = 6639(2) A(3). For the structure solutions of polymorphs A and B, 13 degrees of freedom (3 translational, 3 orientational, 7 torsion angles) were determined in approximately 2 h of computer time, demonstrating that the crystal packing and the molecular conformation of medium-sized (MW approximately 500) pharmaceutical compounds can

now be solved quickly and routinely from high-resolution X-ray powder diffraction data. Copyright 2000 Wiley-Liss, Inc.

L15 ANSWER 15 OF 65 MEDLINE on STN
ACCESSION NUMBER: 2000418692 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 10903938
TITLE: Structure-based drug design: the discovery of novel nonpeptide orally active inhibitors of human renin.
AUTHOR: Rahuel J; Rasetti V; Maibaum J; Rueger H; Goschke R; Cohen N C; Stutz S; Cumin F; Fuhrer W; Wood J M; Grutter M G
CORPORATE SOURCE: Core Technology Area, Novartis Pharma AG, Metabolic and Cardiovascular Diseases, Basle, Switzerland.
SOURCE: Chemistry & biology, (2000 Jul) Vol. 7, No. 7, pp. 493-504. Journal code: 9500160. ISSN: 1074-5521.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200009
ENTRY DATE: Entered STN: 20000915
Last Updated on STN: 20000915
Entered Medline: 20000906

AB BACKGROUND: The aspartic proteinase renin plays an important physiological role in the regulation of blood pressure. It catalyses the first step in the conversion of angiotensinogen to the hormone angiotensin II. In the past, potent peptide inhibitors of renin have been developed, but none of these compounds has made it to the end of clinical trials. Our primary aim was to develop novel nonpeptide inhibitors. Based on the available structural information concerning renin-substrate interactions, we synthesized inhibitors in which the peptide portion was replaced by lipophilic moieties that interact with the large hydrophobic S1/S3-binding pocket in renin. RESULTS: Crystal structure analysis of renin-inhibitor complexes combined with computational methods were employed in the medicinal-chemistry optimisation process. Structure analysis revealed that the newly designed inhibitors bind as predicted to the S1/S3 pocket. In addition, however, these compounds interact with a hitherto unrecognised large, distinct, sub-pocket of the enzyme that extends from the S3-binding site towards the hydrophobic core of the enzyme. Binding to this S3(sp) sub-pocket was essential for high binding affinity. This unprecedented binding mode guided the drug-design process in which the mostly hydrophobic interactions within subsite S3(sp) were optimised. CONCLUSIONS: Our design approach led to compounds with high in vitro affinity and specificity for renin, favourable bioavailability and excellent oral efficacy in lowering blood pressure in primates. These renin inhibitors are therefore potential therapeutic agents for the treatment of hypertension and related cardiovascular diseases.

L15 ANSWER 16 OF 65 BIOSIS COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 2000:364178 BIOSIS Full-text
DOCUMENT NUMBER: PREV200000364178
TITLE: Separation of brompheniramine enantiomers by capillary electrophoresis and study of chiral recognition mechanisms of cyclodextrins using NMR-spectroscopy, UV spectrometry, electrospray ionization mass spectrometry and X-ray crystallography.
AUTHOR(S): Chankvetadze, Bezhan; Burjanadze, Naira; Pintore, Giorgio; Bergenthal, Dieter; Bergander, Klaus; Muehlenbrock, Christoph; Breitkreuz, Joerg; Blaschke, Gottfried [Reprint author]
CORPORATE SOURCE: Institute of Pharmaceutical Chemistry, University of Muenster, Hittorfstrasse 58-62, 48149, Muenster, Germany
SOURCE: Journal of Chromatography A, (April 14, 2000) Vol. 875, No. 1-2, pp. 471-484. print.
CODEN: JOCRAM. ISSN: 0021-9673.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 23 Aug 2000
Last Updated on STN: 8 Jan 2002

AB Opposite migration order was observed for the enantiomers of brompheniramine (N-(3-(4-bromphenyl)-3-(2-pyridyl) propyl)-N,N- dimethylamine) (BrPh) in capillary electrophoresis (CE) when native beta-cyclodextrin (beta-CD) and heptakis(2,3,6-tri-O-methyl)-beta-CD (TM-beta-CD) were used as chiral selectors. NMR spectrometry was applied in order to obtain

information about the stoichiometry, binding constants and structure of the selector-selectand complexes in solution. The data were further confirmed by UV spectrometry and electrospray ionization mass spectrometry. The structure of the complexes in the solid state was determined using X-ray crystallography performed on the co-crystals precipitated from the 1:1 aqueous solution of selector and selectand. This multiple approach allowed an elucidation of the most likely structural reason for a different affinity (binding strength) of BrPh enantiomers towards beta-CD and TM-beta-CD. However, the question about a force responsible for the opposite affinity pattern of BrPh enantiomers towards these CDs could not be answered definitely.

L15 ANSWER 17 OF 65 MEDLINE on STN DUPLICATE 2
ACCESSION NUMBER: 2000187354 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 10720645
TITLE: Antiangiogenic effects of S-nitrosocaptopril crystals as a nitric oxide donor.
AUTHOR: Jia L; Wu C C; Guo W; Young X
CORPORATE SOURCE: La Jolla Pharmaceuticals, 11283 Carmel Creek Rd., San Diego, CA 92130, USA.. lgia@access1.net
SOURCE: European journal of pharmacology, (2000 Mar 10) Vol. 391, No. 1-2, pp. 137-44.
Journal code: 1254354. ISSN: 0014-2999.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200005
ENTRY DATE: Entered STN: 20000518
Last Updated on STN: 20000518
Entered Medline: 20000511

AB Angiogenesis is the formation of new capillaries from preexisting vessels by migration and proliferation of endothelial cells, which produce a cellular signaling messenger, nitric oxide (NO). The purpose of the present study was to examine the effects of exogenous NO donors on angiogenesis by using a novel crystalline NO donor, S-nitrosocaptopril. The characteristic X-ray diffraction pattern of S-nitrosocaptopril was demonstrated for the first time. On primary capillary endothelial cells pretreated with vascular endothelium growth factor (VEGF), S-nitrosocaptopril (1-500 microM), but not captopril, produced a dose-dependent inhibition of endothelial proliferation. On chick embryos of entire living eggs, gelatin sponges adsorbed with VEGF were implanted on the embryo chorioallantoic membrane to promote vascular growth activity within the sponges. Addition of S-nitrosocaptopril crystals (0.1 mg) to the gelatin sponges markedly reduced vascular density around the sponges, whereas captopril did not inhibit neovascularization. The vascular hemoglobin content surrounding each of the gelatin sponges was determined as a confirmatory test. S-nitrosocaptopril, but not captopril, significantly decreased the hemoglobin content of the embryo tissues immediately surrounding the gelatin sponges. In conclusion, S-nitrosocaptopril exerts an inhibitory effect on angiogenesis. This newly discovered function of S-nitrosocaptopril appears to be governed by distinct structural NO moiety.

L15 ANSWER 18 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 2000:796019 CAPLUS Full-text
TITLE: Metallated angiotensin converting enzyme inhibitors: Synthesis and biological applications.
AUTHOR(S): Pandurangi, Raghu S.
CORPORATE SOURCE: Chemistry Department, University of Missouri, Columbia, MO, 65211, USA
SOURCE: Abstracts of Papers, 220th ACS National Meeting, Washington, DC, United States, August 20-24, 2000 (2000) MEDI-022
CODEN: 69FZC3
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal; Meeting Abstract
LANGUAGE: English

AB De novo generation of Angiotensin Converting Enzyme (ACE) has been implicated in the development of tissue fibrosis following myocardial infarction (MI). High d. localization of ACE in infarcted heart and its relationship to tissue repair lead to the development of ACE inhibitors to suppress ACE in vivo. Lisinopril is a clin. approved drug for controlling hypertension and congestive heart failure. Modification of lisinopril by bifunctional chelating agents (BFCAs) carrying diagnostic radiomarker (e.g. 99mTc)

combines high target potential of ACE inhibitors and high noninvasive imaging potential of the radiometal. Synthesis of metalated ACE inhibitors (with rhenium as a surrogate to technetium) poses a challenge to the conformational and biol. activity of native lisinopril. Here, we present a novel synthetic protocol for functionalization of lisinopril by peptidomimitic chelating framework with retention of the inhibitory potency data, followed by the characterization by multinuclide NMR and single crystal X-Ray.

L15 ANSWER 19 OF 65 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 1999435729 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 10504225
TITLE: Crystal structures of alpha-mercaptoacyldipeptides in the thermolysin active site: structural parameters for a Zn monodentation or bidentation in metalloendopeptidases.
AUTHOR: Gaucher J F; Selkti M; Tiraboschi G; Prange T; Roques B P; Tomas A; Fournie-Zaluski M C
CORPORATE SOURCE: Laboratoire de Cristallographie & RMN Biologiques, CNRS EP 2075, UFR des Sciences Pharmaceutiques et Biologiques, 4 Avenue de l'Observatoire, 75270 Paris Cedex 06, France.
SOURCE: Biochemistry, (1999 Sep 28) Vol. 38, No. 39, pp. 12569-76. Journal code: 0370623. ISSN: 0006-2960.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199910
ENTRY DATE: Entered STN: 19991101
Last Updated on STN: 20000303
Entered Medline: 19991020

AB Three alpha-mercaptoacyldipeptides differing essentially in the size of their C-terminal residues have been crystallized in the thermolysin active site. A new mode of binding was observed for 3 [HS-CH(CH(2)Ph)CO-Phe-Tyr] and 4 [HS-CH((CH(2))(4)CH(3))CO-Phe-Ala], in which the mercaptoacyl moieties act as bidentates with Zn-S and Zn-O distances of 2.3 and 2.4 A, respectively, the side chains fitting the S(1), S(1)', and S(2)' pockets. Moreover, a distance of 3.1 A between the sulfur atom and the OE1 of Glu(143) suggests that they are H-bonded and that one of these atoms is protonated. This H-bond network involving Glu(143), the mercaptoacyl group of the inhibitor, and the Zn ion could be considered a "modified" transition state mimic of the peptide bond hydrolysis. Due to the presence of the hindering (5-phenyl)proline, the inhibitor HS-CH(CH(2)Ph)CO-Gly-(5-Ph)Pro (2) interacts through the usual Zn monodentation via the thiol group and occupancy of S(1)' and S(2)' subsites by the aromatic moieties, the proline ring being outside the active site. The inhibitory potencies are consistent with these structural data, with higher affinities for 3 (4.2 x 10(-)(8) M) and 4 (4.8 x 10(-)(8) M) than for 2 (1.2 x 10(-)(6) M). The extension of the results, obtained with thermolysin being considered as the model of physiological zinc metallopeptidases, allows inhibitor-recognition modes for other peptidases, such as angiotensin converting enzyme and neutral endopeptidase, to be proposed and opens interesting possibilities for the design of new classes of inhibitors.

L15 ANSWER 20 OF 65 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1999:629363 SCISEARCH Full-text
THE GENUINE ARTICLE: 228LG
TITLE: 2-benzyl-2-methylsuccinic acid as inhibitor for carboxypeptidase A. Synthesis and evaluation
AUTHOR: Lee M; Jin Y; Kim D H (Reprint)
CORPORATE SOURCE: Pohang Univ Sci & Technol, Ctr Biofunct Mol, San 31 Hyoja Dong, Pohang 790784, South Korea (Reprint); Pohang Univ Sci & Technol, Ctr Biofunct Mol, Pohang 790784, South Korea; Pohang Univ Sci & Technol, Dept Chem, Pohang 790784, South Korea
COUNTRY OF AUTHOR: South Korea
SOURCE: BIOORGANIC & MEDICINAL CHEMISTRY, (AUG 1999) Vol. 7, No. 8, pp. 1755-1760.
ISSN: 0968-0896.
PUBLISHER: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 19

ENTRY DATE: Entered STN: 1999
Last Updated on STN: 1999
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Recently, Asante-Appiah et al. (Asante-Appiah, E.; Seetharaman, J.; Sicheri, F.; Yang, D. S.-C.; Chan, W. W.-C. Biochemistry 1997, 36, 8710-8715) reported that 2-ethyl-2-methylsuccinic acid isa highly potent inhibitor for carboxypeptidase A (CPA), a prototypic zinc protease. The X-ray crystal structure of the complex of the enzyme formed with 2-ethyl-2-methylsuccinic acid revealed that at the active site of CPA there is present a small cavity which accommodates the methyl group of the inhibitor. These investigators postulated that incorporation of a methyl group at the alpha-position to the carboxylate of existing inhibitors of CPA would improve the inhibitory potency. We have synthesized racemic and optically active 2-benzyl-2-methylsuccinic acids and evaluated their inhibitory activities for CPA to find the K-i values to be 0.28, 0.15, and 17 mu M for racemic form, (R)-, and (S)-enantiomer, respectively. Contrary to the expectation, the effect on the binding affinity by the incorporation of the methyl group is minimal. The validity of the proposition that the small cavity may be utilized for the improvement of the inhibitory potency appears questionable.

L15 ANSWER 21 OF 65 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 1999134396 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 9931257
TITLE: The 2.2 A crystal structure of human chymase in complex with succinyl-Ala-Ala-Pro-Phe-chloromethylketone: structural explanation for its dipeptidyl carboxypeptidase specificity.
AUTHOR: Pereira P J; Wang Z M; Rubin H; Huber R; Bode W; Schechter N M; Strobl S
CORPORATE SOURCE: Abteilung fur Strukturforschung, Max-Planck-Institut fur Biochemie, Am Klopferspitz 18a, Martinsried, D-82152, Germany.
CONTRACT NUMBER: AR42931 (NIAMS)
HL50523 (NHLBI)
SOURCE: Journal of molecular biology, (1999 Feb 12) Vol. 286, No. 1, pp. 163-73.
Journal code: 2985088R. ISSN: 0022-2836.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: PDB-1PJP
ENTRY MONTH: 199903
ENTRY DATE: Entered STN: 19990413
Last Updated on STN: 20000303
Entered Medline: 19990329

AB Human chymase (HC) is a chymotrypsin-like serine proteinase expressed by mast cells. The 2.2 A crystal structure of HC complexed to the peptidyl inhibitor, succinyl-Ala-Ala-Pro-Phe-chloromethylketone (CMK), was solved and refined to a crystallographic R-factor of 18.4 %. The HC structure exhibits the typical folding pattern of a chymotrypsin-like serine proteinase, and shows particularly similarity to rat chymase 2 (rat mast cell proteinase II) and human cathepsin G. The peptidyl-CMK inhibitor is covalently bound to the active-site residues Ser195 and His57; the peptidyl moiety juxtaposes the S1 entrance frame segment 214-217 by forming a short antiparallel beta-sheet. HC is a highly efficient angiotensin-converting enzyme. Modeling of the chymase-angiotensin I interaction guided by the geometry of the bound chloromethylketone inhibitor indicates that the extended substrate binding site contains features that may generate the dipeptidyl carboxypeptidase-like activity needed for efficient cleavage and activation of the hormone. The C-terminal carboxylate group of angiotensin I docked into the active-site cleft, with the last two residues extending beyond the active site, is perfectly localized to make a favorable hydrogen bond and salt bridge with the amide nitrogen of the Lys40-Phe41 peptide bond and with the epsilon-ammonium group of the Lys40 side-chain. This amide positioning is unique to the chymase-related proteinases, and only chymases from primates possess a Lys residue at position 40. Thus, the structure conveniently explains the preferred conversion of angiotensin I to angiotensin II by human chymase.

L15 ANSWER 22 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 5
ACCESSION NUMBER: 1998:676010 CAPLUS Full-text

DOCUMENT NUMBER: 130:9978
TITLE: Retention of Inhibitory Potency of an ACE Inhibitor Conjugated with Rh(III) and Pd(II) (Iminophosphorano)phosphines. Synthesis and X-ray Structural Investigations
AUTHOR(S): Pandurangi, Raghoottama S.; Katti, Kattesh V.; Stillwell, Loreen; Barnes, Charles L.
CORPORATE SOURCE: Department of Internal Medicine, University of Missouri, Columbia, MO, 65211, USA
SOURCE: Journal of the American Chemical Society (1998), 120(44), 11364-11373
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Succinimido, amido, and ester functionalized tetrafluoroaryl azides selectively oxidize bisdiphenylphosphinomethane at one of the P(III) centers giving (iminophosphorano)phosphines 6, 7, and 8 resp. in high yields. Succinimido functionalized perfluoroaryl azido (iminophosphorano)phosphine is attached to angiotensin converting enzyme (ACE) inhibitor, lisinopril at one end, leaving the other end for chelation to Rh(III) and Pd(II) precursors including radioactive analogs establishing the hetero-bifunctionality for potential in vivo tracking of the radiotracer. The measurement of inhibitory potency of lisinopril-metal conjugates (Rh and Pd), modified through the primary amine reveals an increase in inhibitory potency, although small, retaining the target potential of native lisinopril toward specific biol. sites. However, direct complexation using the carboxylic groups of lisinopril with a Cu precursor resulted in the reduction of inhibitory potency from nM to μM levels rendering it less useful for applications as an ACE inhibitor. Single-crystal x-ray structural study of the Rh(III) perfluoroaryl (iminophosphorano)phosphine complex 12 shows a distorted mer octahedral configuration with two ligands per metal center and only one of the phosphiniminato N atom coordinating to the metal. Pd(II) complex 18 reveals that the metal is bound to the iminato N atom and the P(III) center via cis disposition to form a five-membered ring. X-ray data for 12.MeCN: triclinic, P.hivin.1, a 11.570(6) Å b 13.668 Å(7) c 20.709(10) Å, α 86.068(10), β 83.774(10), γ 83.503(10)°V = 3229.6(3) Å3, Z = 2, R = 0.028, Rw = 0.050. X-ray data for 18.MeCN: triclinic, P.hivin.1, a 11.457(3) Å, b 12.223(3) Å, c 13.219(4) Å, α 89.98(20), β 73.710(20), γ 69.980(20)°, V = 1665.7(8) Å3, Z = 2, R = 0.024, Rw = 0.031.

REFERENCE COUNT: 102 THERE ARE 102 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 23 OF 65 EMBASE
ACCESSION NUMBER: 1998213362 EMBASE Full-text
TITLE: Synthesis and modelling of novel rigid rods derived from a simple pentacyclic bis-norbornene [1].
AUTHOR: Margetic D.; Johnston M.R.; Tiekink E.R.T.; Warrener R.N.
CORPORATE SOURCE: D. Margetic, Centre for Molecular Architecture, Central Queensland University, Rockhampton, QLD 4702, Australia
SOURCE: Tetrahedron Letters, (16 Jul 1998) Vol. 39, No. 29, pp. 5277-5280. .
Refs: 18
ISSN: 0040-4039 CODEN: TELEAY
PUBLISHER IDENT.: S 0040-4039(98)00999-X
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 14 Aug 1998
Last Updated on STN: 14 Aug 1998

AB New rigid rods with 4σ, 6σ, 10σ, 12σ, and 16σ bond separations have been prepared from the pentacyclic diene 3 using ACE (alkene plus cyclobutene epoxide) and s-tetrazine coupling techniques and their shapes evaluated using AM1 calculations. The X-ray structure of the 6σ-rod 5 is reported.

L15 ANSWER 24 OF 65 SCISEARCH
ACCESSION NUMBER: 1998:764964 SCISEARCH Full-text
THE GENUINE ARTICLE: 126BV

TITLE: Design of mechanism-based carboxypeptidase a inactivators on the basis of the X-ray crystal structure and catalytic reaction pathway
AUTHOR: Lee K J; Kim D H (Reprint)
CORPORATE SOURCE: Pohang Univ Sci & Technol, Dept Chem, San 31 Hyojadong, Pohang 790784, South Korea (Reprint); Pohang Univ Sci & Technol, Dept Chem, Pohang 790784, South Korea; Pohang Univ Sci & Technol, Ctr Biofunct Mol, Pohang 790784, South Korea
COUNTRY OF AUTHOR: South Korea
SOURCE: BIOORGANIC & MEDICINAL CHEMISTRY, (SEP 1998) Vol. 6, No. 9, pp. 1613-1622.
ISSN: 0968-0896.
PUBLISHER: PERGAMON-ELSEVIER SCIENCE LTD, THE BOULEVARD, LANGFORD LANE, KIDLINGTON, OXFORD OX5 1GB, ENGLAND.
DOCUMENT TYPE: Article; Journal
LANGUAGE: English
REFERENCE COUNT: 52
ENTRY DATE: Entered STN: 1998
Last Updated on STN: 1998

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The X-ray crystal structure of the complex of carboxypeptidase A (CPA) and Gly-Tyr, has been documented. The crystal structure reveals that both the amide carbonyl oxygen and the terminal amino nitrogen of Gly-Tyr coordinate to the active site zinc ion of CPA in a bidentate fashion, whereby the zinc-bound water molecule is displaced by the amino group. As to the catalytic mechanism of CPA, it is generally believed that while in the cases of ester substrates the carboxylate of Glu-270 functions as the nucleophile which attacks the scissile carbonyl carbon (anhydride pathway), in the case of peptide substrates the zinc-bound water molecule attacks the scissile peptide bond (general base pathway). In light of the X-ray crystal structure and the proposed catalytic mechanism for the enzyme, it is envisioned that the ester bond of O-(hydroxyacetyl)-L-beta- phenyllactic acid (L-1) would be hydrolyzed by the attack of the carboxylate of Glu-270 to generate an anhydride intermediate. The latter intermediate would then undergo an intramolecular rearrangement initiated by the attack of the hydroxyl to result in to form an ester bond with the Glu-270 carboxylate. This ester formation impairs the catalytic activity of CPA. We have demonstrated using kinetic analysis that L-1 is indeed an inactivator for the enzyme having the k(inact)/K-I value of 0.057 M-1 s(-1). We have also demonstrated that N-(hydroxyacetyl)-L-phenylalanine (L-2) inactivates the enzyme with the k(inact)/K-I value of 0.071 M-1 s(-1), suggesting that the carboxylate becomes to attack the peptide carbonyl carbon to generate the same anhydride intermediate as that formed in the inactivation of CPA by L-1. The formation of the anhydride intermediate rather than a tetrahedral transition state that is expected for peptide type substrates was envisioned to occur on the ground that the zinc-bound water molecule is displaced by the hydroxyl of L-2 upon binding to the enzyme. (C) 1998 Elsevier Science Ltd. All rights reserved.

L15 ANSWER 25 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 6
ACCESSION NUMBER: 1998:378359 CAPLUS Full-text
DOCUMENT NUMBER: 129:136480
TITLE: Structural characterization and solution rotational isomerism of delapril hydrochloride, a dipeptide angiotensin-converting enzyme inhibitor
AUTHOR(S): Redenti, Enrico; Zanol, Margherita; Amari, Gabriele; Ventura, Paolo; Fronza, Giovanni; Bacchi, Alessia; Pelizzi, Giancarlo
CORPORATE SOURCE: Chemical and Biopharmaceutical Department, Chiesi Farmaceutici SpA, Parma, 43100, Italy
SOURCE: Farmaco (1998), 53(3), 214-223
CODEN: FRMCE8; ISSN: 0014-827X
PUBLISHER: Elsevier Science S.A.
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The solid state structure of delapril hydrochloride was determined by single- crystal x-ray diffraction anal. The comparison between delapril and other angiotensin- converting enzyme (ACE) inhibitors of the same family is discussed with regard to the geometry of the phenomenol. active site of the enzyme. In the solid state the amide bond conformation resulted in being trans, whereas, in solution, NMR spectra indicate that the mol. exists as a mixture of rotational isomers trans and cis (approx. 70:30). The free energy of

activation for the hindered rotation about the amide bond was determined by line-shape anal. The attempt to isolate possible conformational polymorphs failed, indicating that the trans conformation is favored when mols. pack together in the crystal.
REFERENCE COUNT: 29 THERE ARE 29 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L15 ANSWER 26 OF 65 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1997:562465 SCISEARCH Full-text
THE GENUINE ARTICLE: XM538
TITLE: gem-Dialkyl succinic acids: A novel class of inhibitors for carboxypeptidases
AUTHOR: AsanteAppiah E (Reprint); Seetharaman J; Sicheri F; Yang D S C; Chan W W C
CORPORATE SOURCE: MCMASTER UNIV, DEPT BIOCHEM, HAMILTON, ON L8N 3Z5, CANADA
COUNTRY OF AUTHOR: CANADA
SOURCE: BIOCHEMISTRY, (22 JUL 1997) Vol. 36, No. 29, pp. 8710-8715
ISSN: 0006-2960.
PUBLISHER: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 30
ENTRY DATE: Entered STN: 1997
Last Updated on STN: 1997
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB gem-Dimethylsuccinic add and its higher homolog, 2-methyl-2- ethylsuccinic acid (MESA) are highly potent inhibitors of both carboxypeptidase A (CPA) and B. The inhibition constant of MESA for CPA (0.11 mu M for the racemic mixture) is remarkable considering the relatively simple structure of the compound. The molecular feature which is crucial for high affinity binding to both carboxypeptidases appears to be the nonpolar gem-dialkyl locus. The structure of the complex between MESA and CPA has been determined by X-ray crystallography to 2.0 Angstrom resolution and shows the R enantiomer of the inhibitor to be bound in a generally substrate-like manner, The carboxymethyl group is coordinated to the Zn ion in the active site, and the gem-dialkyl locus corresponds in position to the alpha-carbon of the C-terminal amino acid in a peptide substrate, The methyl group of the inhibitor occupies a cavity in the enzyme which is apparently not filled upon substrate-binding, We postulate that this cavity (the alpha-methyl hole) is designed to allow the proximal Glu-270 residue to undergo a critical movement during catalysis, The hydrophobic nature of the above cavity may play a role in modulating the reactivity of this residue. These results suggest that similar cenophilic (empty-loving) inhibitors may be found for other enzymes.

L15 ANSWER 27 OF 65 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1997:915825 SCISEARCH Full-text
THE GENUINE ARTICLE: YK964
TITLE: Binuclear copper complexes based on the 6,6'-bis[[bis(2-pyridylmethyl)amino]methyl]-2,2'-bipyridine ligand
AUTHOR: Lee D H (Reprint); Murthy N N; Karlin K D
CORPORATE SOURCE: JOHNS HOPKINS UNIV, DEPT CHEM, BALTIMORE, MD 21218
COUNTRY OF AUTHOR: USA
SOURCE: INORGANIC CHEMISTRY, (3 DEC 1997) Vol. 36, No. 25, pp. 5785-5792.
ISSN: 0020-1669.
PUBLISHER: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: PHYS
LANGUAGE: English
REFERENCE COUNT: 43
ENTRY DATE: Entered STN: 1997
Last Updated on STN: 1997
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The tripodal tetradentate ligand TMPA (tris (2-pyridylmethyl) amine) has provided a wealth of valuable new Cu(I) and Cu(II) chemistry, in particular associated with copper(I)/dioxygen reactivity studies (Karlin, K. D.; Kaderli, S.; Zuberbiihler, A. D. Ace. Chemical Res. 1997, 30, 139-147). Dinucleating analogues have also

been recently investigated, and here we describe new copper complexes of the 6,6'-bis[[bis(2-pyridylmethyl)amino]meth 2,2'-bipyridine ligand(bTMPA). The synthesis and X-ray crystallographic characterization of [(bTMPA)Cu-2(II)(CH3CN)(2)(ClO4)(2)](2+) (1, as ClO4- salt) and [(bTMPA)Cu-2(II)(N-3)(2)(ClO4)(2)] (2) are provided. [1: space group C2/c; a = 15.907(4) Angstrom, b = 29.268(7) Angstrom, c = 13.941(2) Angstrom; beta = 97.79(2)degrees; Z = 4; volume = 6431(2) Angstrom(3). 2: space group P2(1)/c; a = 8.118(5) Angstrom, b = 29.743(8) Angstrom, c = 9.120(6) Angstrom; beta = 114.00(5)degrees; Z = 2; volume = 2012(2) Angstrom(3).] Both solid state structures possess six-coordinate copper(II) ions, and in neither case does the 2,2'-bipyridine (bipy) moiety within bTMPA chelate to a single metal ion. Dissociation of bound perchlorate and the presence of pentacoordinate solution structures are suggested by spectroscopic (UV-vis with two d-d absorptions; axial EPR spectral along with conductivity data (1, 1:4 electrolyte; 2, 1:2 electrolyte). Electrochemical measurements by cyclic volammetry have been carried out, and for a dicopper(I) analogue, [(bTMPA)Cu-2(1)](ClO4)(2)(3(ClO4)(2)), a single quasireversible redox wave is observed; E-1/2 = +199 mV (versus Ag/AgCl in dimethylformamide), which is similar to 280 mV more positive than that observed for the simple ''parent'' compound [Cu-1(TMPA)(CH3CN)I(ClO4). Unlike [Cu-1(TMPA)(CH3CN)](ClO4), 3 does not readily form dioxygen adducts.

L15 ANSWER 28 OF 65 MEDLINE on STN
ACCESSION NUMBER: 97272003 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 9126848
TITLE: Determination of atomic desolvation energies from the structures of crystallized proteins.
AUTHOR: Zhang C; Vasmatzis G; Cornette J L; DeLisi C
CORPORATE SOURCE: Department of Biomedical Engineering, Boston University, MA 02215, USA.
CONTRACT NUMBER: AI30535 (NIAID)
SOURCE: Journal of molecular biology, (1997 Apr 4) Vol. 267, No. 3, pp. 707-26.
Journal code: 2985088R. ISSN: 0022-2836.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: PDB
ENTRY MONTH: 199705
ENTRY DATE: Entered STN: 19970602
Last Updated on STN: 20000303
Entered Medline: 19970519

AB We estimated effective atomic contact energies (ACE), the desolvation free energies required to transfer atoms from water to a protein's interior, using an adaptation of a method introduced by S. Miyazawa and R. L. Jernigan. The energies were obtained for 18 different atom types, which were resolved on the basis of the way their properties cluster in the 20 common amino acids. In addition to providing information on atoms at the highest resolution compatible with the amount and quality of data currently available, the method itself has several new features, including its reference state, the random crystal structure, which removes compositional bias, and a scaling factor that makes contact energies quantitatively comparable with experimentally measured energies. The high level of resolution, the explicit accounting of the local properties of protein interiors during determination of the energies, and the very high computational efficiency with which they can be assigned during any computation, should make the results presented here widely applicable. First we used ACE to calculate the free energies of transferring side-chains from protein interior into water. A comparison of the results thus obtained with the measured free energies of transferring side-chains from n-octanol to water, indicates that the magnitude of protein to water transfer free energies for hydrophobic side-chains is larger than that of n-octanol to water transfer free energies. The difference is consistent with observations made by D. Shortle and co-workers, who measured differential free energies of protein unfolding for site-specific mutants in which Ala or Gly was substituted for various hydrophobic side-chains. A direct comparison (calculated versus observed free energy differences) with those experiments finds slopes of 1.15 and 1.13 for Gly and Ala substitutions, respectively. Finally we compared calculated and observed binding free energies of nine protease-inhibitor complexes. This requires a full free energy function, which is created by adding direct electrostatic interactions and an appropriate entropic component to the solvation free energy term. The calculated free energies are typically within 10% of the observed values. Taken collectively, these results suggest that ACE should provide a reasonably accurate and rapidly evaluatable

solvation component of free energy, and should thus make accessible a range of docking, design and protein folding calculations that would otherwise be difficult to perform.

L15 ANSWER 29 OF 65 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1997:702699 SCISEARCH Full-text
THE GENUINE ARTICLE: XX060
TITLE: QXP: Powerful, rapid computer algorithms for structure-based drug design
AUTHOR: McMartin C (Reprint); Bohacek R S
CORPORATE SOURCE: NOVARTIS PHARMACEUT CORP, RES DEPT, SUMMIT, NJ 07901 USA
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF COMPUTER-AIDED MOLECULAR DESIGN, (JUL 1997) Vol. 11, No. 4, pp. 333-344.
ISSN: 0920-654X.
PUBLISHER: KLUWER ACADEMIC PUBL, SPUIBOULEVARD 50, PO BOX 17, 3300 AA DORDRECHT, NETHERLANDS.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 50
ENTRY DATE: Entered STN: 1997
Last Updated on STN: 1997

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB New methods for docking, template fitting and building pseudo-receptors are described. Full conformational searches are carried out for flexible cyclic and acyclic molecules. QXP (quick explore) search algorithms are derived from the method of Monte Carlo perturbation with energy minimization in Cartesian space. An additional fast search step is introduced between the initial perturbation and energy minimization. The fast search produces approximate low-energy structures, which are likely to minimize to a low energy. For template fitting, QXP uses a superposition force field which automatically assigns short-range attractive forces to similar atoms in different molecules. The docking algorithms were evaluated using X-ray data for 12 protein-ligand complexes. The ligands had up to 24 rotatable bonds and ranged from highly polar to mostly nonpolar. Docking searches of the randomly disordered ligands gave rms differences between the lowest energy docked structure and the energy-minimized X-ray structure, of less than 0.76 Angstrom for 10 of the ligands. For all the ligands, the rms difference between the energy-minimized X- ray structure and the closest docked structure was less than 0.4 Angstrom, when parts of one of the molecules which are in the solvent were excluded from the rms calculation. Template fitting was tested using four ACE inhibitors. Three ACE templates have been previously published. A single run using QXP generated a series of templates which contained examples of each of the three. A pseudo-receptor, complementary to an ACE template, was built out of small molecules, such as pyrrole, cyclo-pentanone and propane. When individually energy minimized in the pseudo-receptor, each of the four ACE inhibitors moved with an rms of less than 0.25 Angstrom. After random perturbation, the inhibitors were docked into the pseudo-receptor. Each lowest energy docked structure matched the energy-minimized geometry with an rms of less than 0.08 Angstrom. Thus, the pseudo-receptor shows steric and chemical complementarity to all four molecules. The QXP program is reliable, easy to use and sufficiently rapid for routine application in structure-based drug design.

L15 ANSWER 30 OF 65 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1997:56121 SCISEARCH Full-text
THE GENUINE ARTICLE: WB915
TITLE: Stereochemistry in inactivation of carboxypeptidase A. Structural analysis of the inactivated carboxypeptidase A by an enantiomeric pair of 2-benzyl-3,4-epoxybutanoic acids
AUTHOR: Ryu S E (Reprint); Choi H J; Kim D H
CORPORATE SOURCE: KOREA RES INST BIOSCI & BIOTECHNOL, PROT ENGN RES DIV, POB 115, TAEJON 305600, SOUTH KOREA (Reprint); POHANG UNIV SCI & TECHNOL, CTR BIOFUNCT MOL, POHANG 790784, SOUTH KOREA; POHANG UNIV SCI & TECHNOL, DEPT CHEM, POHANG 790784, SOUTH KOREA
COUNTRY OF AUTHOR: SOUTH KOREA
SOURCE: JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, (8 JAN 1997)

Vol. 119, No. 1, pp. 38-41.
ISSN: 0002-7863.
PUBLISHER: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: PHYS; LIFE
LANGUAGE: English
REFERENCE COUNT: 41
ENTRY DATE: Entered STN: 1997
Last Updated on STN: 1997
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The X-ray crystal structure of inactivated carboxypeptidase A by (2R,3S)-2-benzyl-3,4-epoxybutanoic acid, a pseudomechanism-based inactivator, was determined to show that the carboxylate of Glu-270 at the active site of the enzyme is covalently modified: the inhibitor is tethered to the carboxylate forming an ester linkage which is brought about by the attack of the carboxylate on the oxirane ring of the inhibitor. Examination of the crystal structure in comparison with that inactivated by its enantiomer, (2S,3R)-2-benzyl-3,4-epoxybutanoic acid, shows that the two inhibitors are bound covalently to the enzyme in a symmetrical fashion. An explanation for the lack of inactivating activity found previously with(2R,3R)- as well as (2S,3S)-2-benzyl-3,4-epoxybutanoic acids was offered.

L15 ANSWER 31 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 7
ACCESSION NUMBER: 1996:494199 CAPLUS Full-text
DOCUMENT NUMBER: 125:184878
TITLE: Three-Dimensional Models of ACE and NEP Inhibitors and Their Use in the Design of Potent Dual ACE/NEP Inhibitors
AUTHOR(S): Bohacek, Regine; De Lombaert, Stephane; McMartin, Colin; Priestle, John; Gruetter, Markus
CORPORATE SOURCE: Pharmaceuticals Division, Ciba-Geigy Corporation, Summit, NJ, 07901, USA
SOURCE: Journal of the American Chemical Society (1996), 118(35), 8231-8249
CODEN: JACSAT; ISSN: 0002-7863
PUBLISHER: American Chemical Society
DOCUMENT TYPE: Journal
LANGUAGE: English

AB A composite template for angiotensin converting enzyme (ACE, EC 2.4.15.1) inhibitors and a hypothetical model of the active site of neutral endopeptidase (NEP, EC 3.4.24.11) have been constructed and used to guide the design of dual ACE/NEP inhibitors. For the ACE template, a new computer program was used to flexibly superimpose potent, conformationally restricted ACE inhibitors. This program, which only considers the structures of the ligands, generated three possible templates. It was possible to evaluate the plausibility of these templates because new x- ray data is extending the authors knowledge of the binding of ligands to zinc metalloproteases. The authors have found that the available x-ray structures of inhibitors complexed to different zinc metalloproteases share certain conformational features. In each complex, the regions between the catalytic zinc and the P1' side chain were found to have almost the same geometry. This geometry appears to be dictated by the mechanism of catalysis. Only one of the templates displays this geometry and is, therefore, proposed as a pharmacophore for ACE. To simulate NEP, the authors used the crystal structure of the active site of thermolysin (EC 3.4.24.4). These models of ACE and NEP predict that the conformation an inhibitor must adopt to bind to ACE differs from that required for binding to NEP. The authors have designed inhibitors in which conformationally restricted sections are linked by a flexible hinge, allowing the mols. to adapt to the conformation required by each enzyme. One of these inhibitors, a tricyclic α-thiol, CGS 28106 (I), was found to inhibit both ACE and NEP with an IC50 of 40 and 48 nM, resp. The models predict that I binds to the S1', S2', and S3' subsites of NEP and thermolysin and to the S1, S1', and S2' subsites of ACE. The predicted mode of binding of I to thermolysin was exptl. verified by the determination of the x-ray crystal structure of the thermolysin/I complex. This is the first reported three-dimensional structure of an α-thiol bound to a zinc metalloprotease. Except for a single NEP inhibitor, the models the authors propose for ACE and NEP are able to differentiate between active and inactive compds. reported in the present as well as other studies of dual ACE/NEP inhibition.

L15 ANSWER 32 OF 65 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1996:548919 SCISEARCH Full-text
THE GENUINE ARTICLE: UY418
TITLE: Structural versatility of peptides from

C-alpha,C-alpha-disubstituted glycines: Crystal -state conformational analysis of peptides from C-alpha-methylhomophenylalanine, (alpha Me)Hph

AUTHOR: Doi M (Reprint); Ishida T; Polese A; Formaggio F; Crisma M; Toniolo C; Broxterman Q B; Kamphuis J

CORPORATE SOURCE: UNIV PADUA, DEPT ORGAN CHEM, CNR, BIOPOLYMER RES CTR, I-35131 PADUA, ITALY; OSAKA UNIV PHARMACEUT SCI, OSAKA 580, JAPAN; DSM RES BV, BIOORGAN CHEM SECT, NL-6160 MD GELEEN, NETHERLANDS

COUNTRY OF AUTHOR: ITALY; JAPAN; NETHERLANDS

SOURCE: INTERNATIONAL JOURNAL OF PEPTIDE AND PROTEIN RESEARCH, (JUN 1996) Vol. 47, No. 6, pp. 491-497. ISSN: 0367-8377.

PUBLISHER: MUNKSGAARD INT PUBL LTD, 35 NORRE SOGADE, PO BOX 2148, DK-1016 COPENHAGEN, DENMARK.

DOCUMENT TYPE: Article; Journal

FILE SEGMENT: LIFE

LANGUAGE: English

REFERENCE COUNT: 68

ENTRY DATE: Entered STN: 1996
Last Updated on STN: 1996

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The molecular and crystal structures of the C-alpha-tetrasubstituted, delta-branched alpha-amino acid C-alpha-methylhomophenylalanine, H-D-(alpha Me)Hph-OH, and three peptides (to the pentamer level), including the homotripeptide, have been determined by X-ray diffraction. The peptides are Z-L-(alpha Me)Hph-(L-Ala)(2)-OMe, pBrBz-[D-(alpha Me)Hph](3)-OtBu and Ac-(Aib)(2)-L-(alpha Me)Hph-(Aib)(2)-OtBu. All the (alpha Me)Hph residues prefer phi,psi torsion angles in the helical region of the conformational map. The two terminally blocked tripeptides adopt a beta-bend conformation stabilized by a 1<--4 C=O ... H-N intramolecular H-bond. The terminally blocked pentapeptide is folded in a regular 3(10)-helix. In general, the relationship between (alpha Me)Hph alpha-carbon chirality and helix handedness is the same as that exhibited by protein amino acids. A comparison is also made with the conclusions extracted from published work on peptides from other types of C-alpha-alkylated aromatic alpha-amino acids. (C) Munksgaard 1996.

L15 ANSWER 33 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1996:414599 CAPLUS Full-text

TITLE: Three-dimensional models for the design of ACE and NEP inhibitors.

AUTHOR(S): Bohacek, Regine; De Lombaert, Stephane; McMartin, Colin; Priestle, John; Grutter, Markus

CORPORATE SOURCE: Research Department, Ciba-Geigy Corporation, Summit, NJ, 07901, USA

SOURCE: Book of Abstracts, 212th ACS National Meeting, Orlando, FL, August 25-29 (1996), MEDI-011. American Chemical Society: Washington, D. C.
CODEN: 63BFAF

DOCUMENT TYPE: Conference; Meeting Abstract

LANGUAGE: English

AB An ACE inhibitor template was constructed using a new computer program which flexibly superimposed four potent, conformationally restricted inhibitors resulting with three possible templates. One of these templates matched the regions between the catalytic zinc and the P1' side chain found in the available X-ray structures of exo- and endo- zinc metalloproteases/inhibitor complexes. This template was proposed as a pharmacophore for ACE. To simulate NEP, we used the crystal structure of the active site of thermolysin. These models were extensively tested with known inhibitors from different labs. and used to guide the design of a tricyclic a-thiol (CGS 28106). The models predict that CGS 28106 binds to the S1', S2' and S3' subsites of NEP and thermolysin and to the S1, S1' and S2' subsites of ACE . The predicted mode of binding to thermolysin was exptl. verified by X-ray crystallog.

L15 ANSWER 34 OF 65 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1995:259419 SCISEARCH Full-text

THE GENUINE ARTICLE: QT032

TITLE: PH, IONIC-STRENGTH, AND TEMPERATURE DEPENDENCES OF IONIZATION EQUILIBRIA FOR THE CARBOXYL GROUPS IN TURKEY OVOMUCOID 3RD DOMAIN

AUTHOR: SCHALLER W (Reprint); ROBERTSON A D
CORPORATE SOURCE: UNIV IOWA, DEPT BIOCHEM, IOWA CITY, IA 52242
COUNTRY OF AUTHOR: USA
SOURCE: BIOCHEMISTRY, (11 APR 1995) Vol. 34, No. 14, pp. 4714-4723

ISSN: 0006-2960.
PUBLISHER: AMER CHEMICAL SOC, PO BOX 57136, WASHINGTON, DC 20037-0136

DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 91
ENTRY DATE: Entered STN: 1995
Last Updated on STN: 1995
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Two-dimensional NMR spectroscopy has been used to monitor the pH dependences of proton chemical shifts for turkey ovomucoid third domain (OMTKY3). Sample pH was varied from 7.0 to 1.4 in order to determine the apparent pK(a), values of all six carboxyl groups in OMTKY3. At 35 degrees C and in the presence of 10 mM KCl, the pK, values for Asp 7, Glu 19, and Asp 27 (<2.6, 3.2, and (<2.3, respectively) are more than 1 pH unit below those for model compounds. The pK, values for Glu 10 (4.1) and Glu 43 (4.7) show more modest deviations from model compound data. The low pK, for the a-carboxyl group of Cys 56 (<2.5) is attributable, at least in part, to acidification by the disulfide group. Fitting the data to a modified Hill equation [Markley, J. L. (1975) Ace, Chemical Res. 8, 70-80] reveals little evidence for interactions between the acidic groups; most Hill coefficients fall between 0.8 and 1.2, with outlying values usually obtained with data that describe incomplete transitions. Most of the very low pK(a) values show increases in the presence of 1.0 M KCl but, with the exception of that for glutamate 19, remain well below model compound values. pH-dependent changes in amide proton chemical shifts permitted identification of hydrogen bonds involving the side chains of Asp 7, Glu 19; and Asp 27, which may partially explain the low pK, values for these groups. These hydrogen bonds, two of which involve side chains that are well exposed to solvent, were previously identified in high-resolution X-ray studies of turkey ovomucoid third domain [Fujinaga, M., Sielecki, A.R., Read, R.J., Ardelt, W., Laskowski, M., Jr., and James, M.N.G. (1987) J. Mol. Biol. 195, 397-418]. Results of additional experiments performed at 15, 25, and 40 degrees C suggest that apparent ionization enthalpies for all carboxyl groups in OMTKY3 are about 0 +/- 2 kcal/mol. In the accompanying paper [Swint, L., and Robertson, A.D. (1995) Biochemistry 34, 4724-4732], the pH dependence of OMTKY3 stability is described and compared to expectations based on the pK(a) values described herein.

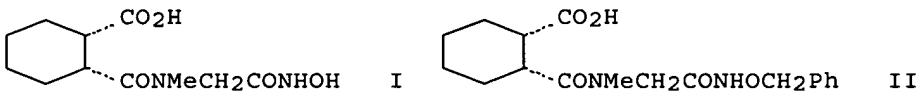
L15 ANSWER 35 OF 65 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1995:335156 SCISEARCH Full-text
THE GENUINE ARTICLE: QX798
TITLE: GENERATION AND REACTIVITY OF CP-ASTERISK-W(NO)(CH(2)SIME(3))H, A 16-VALENCE-ELECTRON ALKYL HYDRIDE COMPLEX
AUTHOR: DEBAD J D (Reprint); LEGZDINS P; LUMB S A; BATCHELOR R J; EINSTEIN F W B
CORPORATE SOURCE: UNIV BRITISH COLUMBIA, DEPT CHEM, 2036 MAIN MALL, VANCOUVER, BC V6T 1Z1, CANADA (Reprint); SIMON FRASER UNIV, DEPT CHEM, BURNABY, BC V5A 1S6, CANADA
COUNTRY OF AUTHOR: CANADA
SOURCE: ORGANOMETALLICS, (MAY 1995) Vol. 14, No. 5, pp. 2543-2555.
ISSN: 0276-7333.
PUBLISHER: AMER CHEMICAL SOC, PO BOX 57136, WASHINGTON, DC 20037-0136

DOCUMENT TYPE: Article; Journal
FILE SEGMENT: PHYS
LANGUAGE: English
REFERENCE COUNT: 48
ENTRY DATE: Entered STN: 1995
Last Updated on STN: 1995
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Treatment of solutions of Cp*W(NO)(CH(2)SiMe(3))(2) with H-2 generates in situ the reactive 16-valence-electron alkyl hydride Cp*W(NO)(CH(2)SiMe(3))H, formed by hydrogenolysis of one of the W-C sigma-bonds of the dialkyl reactant. The Lewis-acidic hydride complex has not yet been isolated, but its existence has been

inferred on the basis of the varied chemical reactions that it undergoes when generated in the presence of reactive substrates. PPh(3) affords the orthometalated complex Cp*W(NO)(H)(PPh(2)C(6)H(4)) as a yellow crystalline solid probably via the 18-electron adduct Cp*W(NO)(CH(2)SiMe(3))(PPh(3))H. Consistently, the same reaction effected with PPh(3)-d(15) results in complete deuteration of the hydride position in the product. Acyclic, conjugated dienes such as butadiene or 2,3-dimethyl-1,3-butadiene afford Cp*W(NO)(eta(4)-trans-diene) complexes. The characteristic chemistry of Cp*W(NO)(CH(2)SiMe(3))H is, however, dominated by the ability of its W-H link to insert unsaturated linkages, the regioselectivity of the insertions indicating that the hydride Ligand is hydridic in nature. For instance, insertion of acetonitrile affords the ethylideneamido complex Cp(*)W(NO)(CH(2)SiMe(3))(N=CHMe), which is isolable as a diastereomeric pair. Similarly, insertions of organic reagents containing carbonyl (O=C) or imine (HN=C) functional groups produce the corresponding alkyl alkoxide or alkyl amide products, respectively, in virtually quantitative yields. Phenylacetylene affords the novel alkyl alkenyl compound Cp*W(NO)(CH(2)SiMe(3))(CPh=CH2), which is thermally unstable and isolable in only low yields. Insertions into the W-H bond by other olefinic substrates are successful only if the unsaturated hydrocarbon also contains a Lewis-base functional group. Thus, propargylamine and allylamine produce the related metallacyclic complexes Cp*W(NO)(CH(2)SiMe(3))(NH2CH2CHCH) and Cp*W(NO)(CH(2)SiMe(3))(NH2CH2CH2CH2), respectively. Treatment of Cp*W(NO)(CH(2)SiMe(3))(2) with H-2 in the presence of allyl alcohol does not produce an oxometallacycle, but rather affords the allylalkoxo complex resulting from the alcohol simply functioning as a protonic acid toward the dialkyl reactant. The solid-state molecular structures of Cp*W(NO)(CH(2)SiMe(3))(N=CHMe) and Cp*W(NO)(CH(2)SiMe(3))(NH2CH2CH2CH2) have been established by single- crystal X-ray crystallographic analyses. Crystals of Cp*W(NO)(CH(2)SiMe(3))(N=CHMe) are monoclinic of space group P2(1)/n: a = 9.515(2) Angstrom; b = 21.946(3) Angstrom; c = 9.552(2) Angstrom; Z = 4; V = 1946.8 Angstrom(3); T = 200 K; R(f) = 0.029 for 2035 data (I-0 greater than or equal to 2.5 sigma(I-0)) and 106 variables. Crystals of Cp*W(NO)(CH(2)SiMe(3))(NH2CH2CH2CH2) are orthorhombic of sp ace group P2(1)2(1)2(1): a 11.417(4) Angstrom; b = 13.178(2) Angstrom; c 13.804(4) Angstrom; Z = 4; V = 2076.9 Angstrom(3); T = 200 K; R(f) = 0.020 for 2420 data (I-0 greater than or equal to 2.5 sigma(I-0)) and 208 variables.

L15 ANSWER 36 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 8
ACCESSION NUMBER: 1995:434524 CAPLUS Full-text
DOCUMENT NUMBER: 122:290088
TITLE: Structure and conformation of (1S,2R)-cis-2-[hydroxyaminocarbonylmethyl(N-methyl)aminocarbonyl]cyclohexanecarboxylic acid: x-ray, NMR and molecular mechanics studies
AUTHOR(S): Di Bugno, Cristina; Colombani, Spartaco Mauro; Dapporto, Paolo; Giorgi, Raffaello; Paoli, Paola
CORPORATE SOURCE: Laboratori Guidotti S.p.A., Pisa, 56122, Italy
SOURCE: Journal of the Chemical Society, Perkin Transactions 2: Physical Organic Chemistry (1995), (3), 609-13
CODEN: JCPKBH; ISSN: 0300-9580
PUBLISHER: Royal Society of Chemistry
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB The structural characterization of idrapril, (1S,2R)-cis-2- [hydroxyaminocarbonylmethyl(N-methyl)-aminocarbonyl]cyclohexanecarboxylic acid (I), a novel ACE inhibitor and its related benzyloxy derivative (II) has been carried out by NMR studies. The crystal structure of II has been determined by x-ray diffraction. The NMR spectra indicate the presence of two cis and trans isomers with respect to the amide bond at room temperature, with rotational barriers of 70 kJ mol-1. The preferred conformation of these compds. is

the trans rotamer with the carboxylic moiety in the equatorial orientation. Conformational studies in aqueous solution have been reported for idrapril as a function of pH and the equilibrium constant has been determined The results suggest the presence of intramol. hydrogen bonds, as is confirmed by mol. mechanics calcns.

L15 ANSWER 37 OF 65 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1995:549641 SCISEARCH Full-text
THE GENUINE ARTICLE: RP971
TITLE: ZINC-DIRECTED INHIBITORS FOR ZINC PROTEINASES
AUTHOR: FEINBERG H (Reprint); GREENBLATT H M; BEHAR V; GILON C; COHEN S; BINO A; SHOHAM G
CORPORATE SOURCE: HEBREW UNIV JERUSALEM, INST CHEM, IL-91904 JERUSALEM, ISRAEL; HEBREW UNIV JERUSALEM, STRUCT CHEM & BIOL LAB, IL-91904 JERUSALEM, ISRAEL
COUNTRY OF AUTHOR: ISRAEL
SOURCE: ACTA CRYSTALLOGRAPHICA SECTION D-BIOLOGICAL CRYSTALLOGRAPHY, (1 JUL 1995) Vol. 51, Part 4, pp. 428-449

ISSN: 0907-4449.
PUBLISHER: MUNKSGAARD INT PUBL LTD, 35 NORRE SOGADE, PO BOX 2148, DK-1016 COPENHAGEN, DENMARK.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: PHYS; LIFE
LANGUAGE: English
REFERENCE COUNT: 105
ENTRY DATE: Entered STN: 1995
Last Updated on STN: 1995
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Zinc proteinases have been recognized as a distinct class of proteolytic enzymes in which at least one ion of zinc is involved directly in catalysis. This family includes a growing number of biologically important enzymes which are attractive targets for rational drug design. In this paper we examine the special features of the zinc binding environment of these enzymes in order to gain information which could be useful in the preparation of 'zinc-directed' selective inhibitors. Carboxypeptidase A (CPA) is presented as a model for one class of zinc proteinases, and the active-site zinc and its interactions are examined with the primary focus on geometrical considerations. The three-dimensional structure of the native and apoenzyme are discussed, together with the high-resolution structure of several enzyme-inhibitor complexes. This paper will first present a structural analysis of CPA derivatives and then discuss a series of zinc model compounds which have been prepared and characterized in order to examine the ligand and geometrical preferences of the zinc in an unstrained system. X- ray crystallography (macromolecular and small molecule) is the main experimental method used for the structural analyses, while complementary computational methods have been used for the examination of electrostatic potentials. The results from the various experimental efforts are assembled in order to draw general conclusions on the potential use of the zinc ion as the primary target for inhibitor binding. The results of these studies suggest that the zinc ion is important for both the binding and the catalytic activation of the substrate as well as for stabilization of the tetrahedral reaction intermediate.

L15 ANSWER 38 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN

ACCESSION NUMBER: 1995:214238 CAPLUS Full-text
DOCUMENT NUMBER: 122:176893
TITLE: Influence of the Alkoxide Moiety on Heterometallic Compound Formation: Structure and Dynamics of KZr2(OtBu)9 and K2Zr2(OtBu)10
AUTHOR(S): Teff, Daniel J.; Huffman, John C.; Caulton, Kenneth G.
CORPORATE SOURCE: Molecular Structure Center, Indiana University, Bloomington, IN, 47405-4001, USA
SOURCE: Inorganic Chemistry (1994), 33(26), 6289-92
CODEN: INOCAJ; ISSN: 0020-1669
DOCUMENT TYPE: Journal
LANGUAGE: English

AB KZr2(OtBu)9 was prepared by reaction of KOtBu with ZFR(OtBu)4 in a 1:2 molar ratio. Attempted sublimation results in dissociation of Zr(OtBu)4, affording [KZr(OtBu)5]n, which can also be synthesized using equimolar KOtBu and Zr(OtBu)4. Single-crystal x-ray diffraction revealed that n = 2; K2Zr2(OtBu)10 crystallizers from pentane at -20°C in the

monoclinic space group P21/c, with unit cell dimensions a = 10.532(1) Å, b = 18.057(3) Å, c = 27.618(5) Å, β = 95.54(1)° and Z = 4. The dimer is composed of two five-coordinate Zr centers, each having trigonal bipyramidal geometry; the aces of the trigonal bipyramids are orthogonal, and the Zr(OtBu)5- units encapsulated both potassiums. Due to fluxionality, this species appears as a singlet in 1H NMR in d8-toluene even at -75°C. Interconversions between and possible dissociative reactions of KZr2(OtBu)9 and [KZr(OtBu)5]2 are also tested exptl.

L15 ANSWER 39 OF 65 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1994:97809 SCISEARCH Full-text
THE GENUINE ARTICLE: MW990
TITLE: [FE(OME)(2)(O2CCH2CL)](10), A MOLECULAR FERRIS WHEEL
AUTHOR: TAFT K L (Reprint); DELFS C D; PAPAEFTHYMIOU G C; FONER S; GATTESCHI D; LIPPARD S J
CORPORATE SOURCE: UNIV FIRENZE, DIPARTIMENTO CHIM, I-50144 FLORENCE, ITALY; MIT, DEPT CHEM, CAMBRIDGE, MA 02139; MIT, FRANCIS BITTER NATL MAGNET LAB, CAMBRIDGE, MA 02139; MIT, DEPT PHYS, CAMBRIDGE, MA 02139
COUNTRY OF AUTHOR: ITALY; USA
SOURCE: JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, (9 FEB 1994) Vol. 116, No. 3, pp. 823-832. ISSN: 0002-7863.
PUBLISHER: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036.
DOCUMENT TYPE: General Review; Journal
FILE SEGMENT: PHYS; LIFE
LANGUAGE: English
REFERENCE COUNT: 101
ENTRY DATE: Entered STN: 1994
Last Updated on STN: 1994

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The synthesis of [Fe(OMe)(2)(O2CCH2Cl)](10), a molecular ferric wheel, from basic iron chloroacetate and ferric nitrate in methanol is described. Spectroscopic analysis of methanol solutions used to prepare the compound revealed a (mu-oxo)(mu-carboxylato)diiron(III) intermediate having terminal oxygen donor ligands. The structure of the crystalline ferric wheel was revealed in a single crystal X- ray diffraction investigation. The molecule has idealized D-5d symmetry and consists of a 20-membered ring comprised of 10 ferric ions linked by 20 bridging methoxide and 10 bridging chloroacetate ligands. The 10 iron atoms ace approximately coplanar and are coordinated in a distorted octahedral manner by 6 oxygen donor atoms. Quantitative analysis of the geometry indicated that the curvature arises from a combination of convex bending by 205 degrees (interior angle) across the bridging,methoxides and concave bending. by 119 degrees (interior angle) at the iron atoms. The Mossbauer spectrum of a polycrystalline sample of the ferric wheel at 4.2 K consisted of a single quadrupole split doublet with delta = 0.52 mm s(-1) and Delta E(Q) = 0.62 mm s(-1). The solid state magnetic properties of the compound were extensively investigated. The T-chi value decreased from 32.3 emu mol(-1) K at 300 K to 0.355 emu mol(-1) K at 2.5 K, consistent with antiferromagnetic exchange coupling. The temperature dependence of the susceptibility could be adequately fit by a classical linear chain treatment down to 50 K with a nearest-neighbor coupling constant of similar to 10 cm(-1), where H = JS(i).S-i+1, and g = 2.0. In order to account for the temperature dependence over the entire temperature range,the Heisenberg-Dirac-van Vleck spin Hamiltonian was applied and solved numerically for a ring of eight iron(III) ions an approach that gave J = 9.6 cm(-1) with g = 2.0, and an excellent fit to the experimental data. The low-lying states of th spin manifold were dramatically revealed by high-field DC and pulsed magnetization measurements at 0.6 K. The reduced magnetization increased in discrete steps with evenly spaced increments in the magnetic field, a result that was quantitatively accounted for by the theoretical spin manifold.

L15 ANSWER 40 OF 65 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1994:295242 SCISEARCH Full-text
THE GENUINE ARTICLE: NK136
TITLE: IMPACT OF MASS-SPECTROMETRY IN SURFACE-ANALYSIS
AUTHOR: VICKERMAN J C (Reprint)
CORPORATE SOURCE: UMIST, DEPT CHEM, SURFACE ANAL RES CTR, MANCHESTER M60 1QD, ENGLAND (Reprint)
COUNTRY OF AUTHOR: ENGLAND

SOURCE: ANALYST, (APR 1994) Vol. 119, No. 4, pp. 513-523.
ISSN: 0003-2654.
PUBLISHER: ROYAL SOC CHEMISTRY, THOMAS GRAHAM HOUSE, SCIENCE PARK MILTON ROAD, CAMBRIDGE, CAMBS, ENGLAND CB4 4WF.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: PHYS; LIFE
LANGUAGE: English
REFERENCE COUNT: 47
ENTRY DATE: Entered STN: 1994
Last Updated on STN: 1994
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The surface scientist has a wide range of sophisticated techniques available to study the state of surfaces and molecules adsorbed thereon. On single crystals the surface geometry and structural and electronic state of the surface and simple adsorbates can be probed precisely. On less ideal surfaces, many of the techniques are very difficult to apply. Amongst the armoury of surface science techniques, only two have produced significant fruit in the study of chemically complex materials: X-ray photoelectron spectroscopy (XPS) and static secondary ion mass spectrometry (SSIMS). Although XPS has been, and continues to be, very important as the most widely used method of surface analysis, in many applications of current interest SSIMS is proving to have tremendous potential and could develop into the technique of choice for a vast range of problems. Chief amongst its strengths is its emerging ability to provide chemical structure data in the form of the cluster or polyatomic ions which are observed. The emergence of SSIMS as a true surface mass spectrometric technique for the analysis of complex materials is reviewed and the following aspects are demonstrated: SSIMS is basically a soft ionization technique where the spectra are related to the surface chemical structure; organic and other insulating materials can be analysed easily; and time-of-flight analysers ace the analysers of choice for most SSIMS analyses.

L15 ANSWER 41 OF 65 EMBASE COPYRIGHT (c) 2006 Elsevier B.V. All rights reserved on STN
ACCESSION NUMBER: 94360991 EMBASE Full-text
DOCUMENT NUMBER: 1994360991
TITLE: 11-fold symmetry of the trp RNA-binding attenuation protein (TRAP) from bacillus subtilis determined by X-ray analysis.
AUTHOR: Antson A.A.; Brzozowski A.M.; Dodson E.J.; Dauter Z.; Wilson K.S.; Kurecki T.; Otridge J.; Gollnick P.
CORPORATE SOURCE: Department of Biological Sciences, Cooke Hall, State University of New York,Buffalo, NY 14260, United States
SOURCE: Journal of Molecular Biology, (1994) Vol. 244, No. 1, pp. 1-5. .
ISSN: 0022-2836 CODEN: JMOBAK
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 29 Dec 1994
Last Updated on STN: 29 Dec 1994

AB The trp, RNA-binding attenuation protein (TRAP) of Bacillus sbbtilis has been crystallized and examined by crystallography using X- ray synchrotron radiation diffraction data. Crystals of TRAP complexed with L-tryptophan belong to sp ace group C2 with a 156.8 Å, b = 114.05 Å, c = 105.9 Å, β = 118.2°. Crystals of a potential heavy-atom derivative of TRAP complexed with 5-bromo-L-tryptophan grow in the same space group with similar cell dimensions. X ray data for the native crystals and for the derivative have been collected to 2.9 Å and 2.2 Å resolution, respectively. Peaks in the self-rotation function and in the Patterson synthesis could only be explained by two 11-subunit oligomers (each formed by an 11-fold axis of symmetry) in the asymmetric unit lying with the 11-fold rotation axes parallel to each other. The consequence is that the TRAP molecule has 11-fold symmetry and contains 11 subunits.

L15 ANSWER 42 OF 65 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1993:382495 SCISEARCH Full-text
THE GENUINE ARTICLE: LG158
TITLE: COORDINATION AND OLIGOMERIZATION OF ALKYNES AT MONONUCLEAR TUNGSTEN ARYLOXIDE METAL CENTERS

AUTHOR: KRILEY C E (Reprint); KERSCHNER J L; FANWICK P E; ROTHWELL I P
CORPORATE SOURCE: PURDUE UNIV, DEPT CHEM, 1393 BROWN BLDG, W LAFAYETTE, IN 47907
COUNTRY OF AUTHOR: USA
SOURCE: ORGANOMETALLICS, (JUN 1993) Vol. 12, No. 6, pp. 2051-2058. ISSN: 0276-7333.
PUBLISHER: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036.
DOCUMENT TYPE: General Review; Journal
FILE SEGMENT: PHYS
LANGUAGE: English
REFERENCE COUNT: 98
ENTRY DATE: Entered STN: 1994
Last Updated on STN: 1994

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB Reduction of either [W(OC6H3Ph2-2,6)2Cl4] (OCH3Ph2-2,6 = 2,6-diphenylphenoxide) or [W(OC6H3Pri2-2,6)2Cl4] (OC6H3Pri2-2,6 = 2,6-diisopropylphenoxide) in toluene with sodium amalgam in the presence of alkynes (EtC=CEt; PhC=CPh; 4Me-PhC=CPh-4Me) leads to a series of alkyne (ac) adducts of general formulae [(ArO)2WCl2(ac)] (1) and [(ArO)2W(ac)2] (2). The C-13 NMR spectra of 1 and 2 show downfield shifts for the coordinated alkyne carbon atoms. A single crystal X- ray diffraction analysis shows five coordinate [W(OC6H3Ph2-2,6)2Cl2(C2Et2)] (1a) to adopt a square pyramidal geometry about tungsten with trans aryloxide ligands and an axial 3-hexyne. The solid state structure of [W(OC6H3Ph-2,6)2(C2Et2)2] (2a) shows a pseudo-tetrahedral environment about tungsten with the two 3-hexyne ligands arranged parallel with each other. Reaction of the eta6-arene complex [W(OC6H3Ph-eta6-C6H5)(OC6H3Ph2-2,6)(dppm)] with 3-hexyne generates the compound [W(OC6H3Ph2-2,6)2(C4Et4)] (3) which contains a tunptacyclopentatriene ring. This ring is nonplanar both in the solid state and solution (NMR). The bis-cyclometalated compounds [W(OC6H3Ph-C6H4)2(L)2] (L = PMe2Ph, PMePh2, and py) react with alkynes to form a number of products. From the reaction with 3-hexyne, two new compounds of formula [W(OC6H3PhC6H4)2(C4Et4)] (4) and [W(OC6H3PhC6H4)2(C6Et6)] (5) were isolated. Structural studies on 4 and 5 show them to contain multiple metallacyclic rings formed by transfer of one of the metalated aryloxide carbon atoms to an alpha-carbon of an intermediate tungstacyclopenta-2,4-diene complex. Crystal data at -100-degrees-C for WCl2O2C42H36 (1a): a = 9.331(2), b = 12.271(2), c = 16.334(3) angstrom; alpha = 107.48(1), beta = 101.78(2), gamma = 95.13(2)-degrees; Z = 2, d(calcd) = 1.595 g cm-3 in space group P1BAR; for WO2C48H46 (2a) at 20-degrees-C: a = 11.458(1), b = 17.961(4), c = 10.915(2) angstrom; alpha = 104.65(1), beta = 115.23(1), gamma = 92.08(1)-degrees; Z = 2, d(calcd) = 1.437 g CM-3 in ace group P1BAR; for WO2C48H46 (3) at -114-degrees-C: a = 11.086(2), b = 18.400(7), c = 19.453(5) angstrom alpha = 98.96(2), beta = 97.14(2), gamma = 98.67(2)-degrees; Z = 4, d(calcd) = 1.454 g cm-3 in space group P1BAR; for WO2C48H44 (4) at 20-degrees-C: a = 10.805(7), b = 11.662(1), c = 17.008(3) angstrom; alpha = 80.12(1), beta = 84.71(3), gamma = 63.07(3)-degrees; Z = 2, d(calcd) = 1.476 g cm-3 in space group Pi; for WO2C54H54 (5) at 20-degrees-C: a = 9.835(2), b = 11.8298(7), c = 19.620(2) angstrom; alpha = 104.748(6), beta = 98.717(9), gamma = 104.478-(8)-degrees; Z = 2, d(calcd) = 1.467 g cm-3 in space group P1BAR.

L15 ANSWER 43 OF 65 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1994:485573 SCISEARCH Full-text
THE GENUINE ARTICLE: BZ58Z
TITLE: DETECTING METAL-METAL INTERACTIONS AND MEASURING DISTANCES BETWEEN METAL CENTERS IN METALLOPROTEINS
AUTHOR: MARET W (Reprint)
CORPORATE SOURCE: HARVARD UNIV, SCH MED, CTR BIOCHEM & BIOPHYS SCI & MED, BOSTON, MA 02115 (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: METALLOBIOCHEMISTRY, PART C, (1993) Vol. 226, Part C, pp. 594-618. ISSN: 0076-6879.
PUBLISHER: ACADEMIC PRESS INC, 525 B STREET, SUITE 1900, SAN DIEGO, CA 92101-4495.
DOCUMENT TYPE: General Review; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 118
ENTRY DATE: Entered STN: 1994
Last Updated on STN: 1994

L15 ANSWER 44 OF 65 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1993:352098 SCISEARCH Full-text
THE GENUINE ARTICLE: LE407
TITLE: STRUCTURAL STUDIES OF THE ROLE OF THE ACTIVE-SITE METAL IN METALLOENZYMES
AUTHOR: FEINBERG H (Reprint); GREENBLATT H M; SHOHAM G
CORPORATE SOURCE: HEBREW UNIV JERUSALEM, DEPT INORGAN CHEM, IL-91904 JERUSALEM, ISRAEL; HEBREW UNIV JERUSALEM, STRUCT CHEM & BIOL LAB, IL-91904 JERUSALEM, ISRAEL
COUNTRY OF AUTHOR: ISRAEL
SOURCE: JOURNAL OF CHEMICAL INFORMATION AND COMPUTER SCIENCES, (MAY-JUN 1993) Vol. 33, No. 3, pp. 501-516. ISSN: 0095-2338.
PUBLISHER: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: PHYS
LANGUAGE: English
REFERENCE COUNT: 85
ENTRY DATE: Entered STN: 1994
Last Updated on STN: 1994
ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB This paper describes several experimental and computational methods which are currently used in the structural analysis of metal-containing macromolecules. A specific family of proteolytic enzymes which contain a zinc cation in the active site was selected to demonstrate these methods. A range of studies using one example from this family of enzymes is described which serves to clarify the role of the metal in the overall protein structure and in the local conformation of the active site in the native enzyme, the metal-deficient enzyme, and the metal-substituted enzyme and in complexes of the enzyme with various chemical analogues. The main experimental method described is X-ray crystallography, while computational methods for the examination of surface interactions and electrostatic potential effects are described briefly to complement the structural conclusions. The various experimental and computational results are, then assembled in order to draw general conclusions on the structure-function relationships of metalloproteins and in particular the role of the metal in metal-containing proteolytic enzymes. The results of these studies implicate the zinc ion in the binding and catalytic activation of the substrate and stabilization of the tetrahedral reaction intermediate. It appears that in this family of enzymes a divalent metal cation is important for the required catalytic arrangement of functional groups in the active site, especially the metal ligands. However, once an appropriate metal ion is coordinated, there is practically no effect of the particular metal ion bound on either the overall three dimensional structure of the enzyme or the local detailed structure of its active site.

L15 ANSWER 45 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:573436 CAPLUS Full-text
DOCUMENT NUMBER: 119:173436
TITLE: Drug design based on the three-dimensional structure
AUTHOR(S): Hata, Tadashi
CORPORATE SOURCE: Anal. Metab. Res. Lab., Sankyo Co., Ltd., Tokyo, 140, Japan
SOURCE: Nippon Kessho Gakkaishi (1993), 35(1), 7-13 CODEN: NKEGAF; ISSN: 0369-4585
DOCUMENT TYPE: Journal; General Review
LANGUAGE: Japanese

AB A review, with 9 refs., on the 3-dimensional (D) arrangement of the topog. pharmacophoric pattern reflecting the 2-D matrix comprised of the interat. distances of the pattern, the geometrical matching system utilizing the 2-D matrix, application of the system to the study of angiotensin -converting enzyme inhibitors and anti-inflammatory drugs in Cambridge crystal data, and pharmacol. screening by x-ray structure anal.

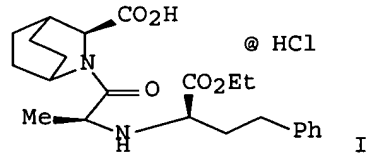
L15 ANSWER 46 OF 65 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1992:567212 SCISEARCH Full-text
THE GENUINE ARTICLE: JP593
TITLE: STRUCTURAL COMPARISON OF SULFODIIMINE AND SULFONAMIDE INHIBITORS IN THEIR COMPLEXES WITH ZINC ENZYMES

AUTHOR: CAPPALONGA A M (Reprint); ALEXANDER R S; CHRISTIANSON D W
CORPORATE SOURCE: UNIV PENN, DEPT CHEM, PHILADELPHIA, PA 19104 (Reprint)
COUNTRY OF AUTHOR: USA
SOURCE: JOURNAL OF BIOLOGICAL CHEMISTRY, (25 SEP 1992) Vol. 267, No. 27, pp. 19192-19197.
ISSN: 0021-9258.
PUBLISHER: AMER SOC BIOCHEMISTRY MOLECULAR BIOLOGY INC, 9650 ROCKVILLE PIKE, BETHESDA, MD 20814.
DOCUMENT TYPE: Article; Journal
FILE SEGMENT: LIFE
LANGUAGE: English
REFERENCE COUNT: 48
ENTRY DATE: Entered STN: 1994
Last Updated on STN: 1994

ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The three-dimensional structure of (L(-)-2-carboxy-3-phenylpropyl) methylsulfodiimine in its complex with the zinc metalloenzyme carboxypeptidase A has been determined at 2.25-angstrom resolution by x-ray crystallographic methods. This is the first example of a sulfodiimine-containing inhibitor binding to a zinc enzyme, and the structure of the enzyme-inhibitor complex reveals that the tetrahedral sulfodiimine group coordinates to the active site zinc ion in unidentate fashion. The zinc-coordinated nitrogen atom of the sulfodiimine group is also within hydrogen bonding distance to active site base Glu-270; presumably, the sulfodiimine is ionized and accepts a hydrogen bond from protonated Glu-270. The other sulfodiimine nitrogen accepts a hydrogen bond from Arg-127, and the inhibitor binds as a possible analogue of the tetrahedral transition state (or intermediate) in a promoted water pathway for peptide hydrolysis. The unidentate sulfodiimine-zinc binding mode observed in this enzyme-inhibitor complex is reminiscent of that observed in sulfonamide complexes with the zinc metalloenzyme carbonic anhydrase II, and the structural features of sulfodiimine- and sulfonamide-zinc interactions exhibit important similarities among recently determined structures of enzyme-inhibitor complexes: ionized nitrogens bind to zinc in each structure, and these nitrogens are engaged in hydrogen bond interactions with neighboring enzyme residues.

L15 ANSWER 47 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1993:124977 CAPLUS Full-text
DOCUMENT NUMBER: 118:124977
TITLE: Synthesis and conformational studies of Zabicipril (S 9650-3), a potent inhibitor of angiotensin converting enzyme
AUTHOR(S): Vincent, Michel; Pascard, Claudine; Cesario, Michele; Remond, Georges; Bouchet, Jean Paul; Charton, Yves; Laubie, Michel
CORPORATE SOURCE: Inst. Rech. Sevier, Suresnes, 92150, Fr.
SOURCE: Tetrahedron Letters (1992), 33(48), 7369-72
CODEN: TELEAY; ISSN: 0040-4039
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 118:124977
GI



I

AB The synthesis of the title compound I is described. The inhibitor of Angiotensin Converting Enzyme (ACE) contains 2-azabicyclo[2.2.2]octanecarboxylic acid, a bulky cyclic amino acid replacing the proline moiety present in most ACE inhibitors described in the literature. Structural anal. of I supports the hypothesis of preferred conformations for

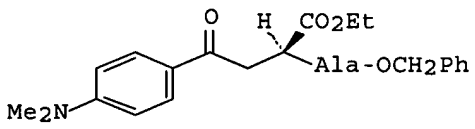
this type of pseudo peptidic mol., in solution (1H, 13C NMR) and in the solid state (x-ray).

L15 ANSWER 48 OF 65 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 1992:183013 SCISEARCH Full-text
THE GENUINE ARTICLE: HJ253
TITLE: X-RAY CRYSTALLOGRAPHIC STUDY OF COVALENTLY MODIFIED CARBOXYPEPTIDASE-A BY 2-BENZYL-3,4-EPOXYBUTANOIC ACID, A PSEUDOMECHANISM-BASED INACTIVATOR
AUTHOR: YUN M Y (Reprint); PARK C Y; KIM S S; NAM D Y; KIM S C; KIM D H
CORPORATE SOURCE: LUCKY LTD, CTR RES & DEV, POB 10 DAE DEOG DANJI, TAEJON 305343, SOUTH KOREA; POHANG INST SCI & TECHNOL, DEPT CHEM, POHANG 790600, SOUTH KOREA; POHANG INST SCI & TECHNOL, CTR BIOFUNCT MOLECULES, POHANG 790600, SOUTH KOREA
COUNTRY OF AUTHOR: SOUTH KOREA
SOURCE: JOURNAL OF THE AMERICAN CHEMICAL SOCIETY, (11 MAR 1992) Vol. 114, No. 6, pp. 2281-2282. ISSN: 0002-7863.
PUBLISHER: AMER CHEMICAL SOC, 1155 16TH ST, NW, WASHINGTON, DC 20036.
DOCUMENT TYPE: Note; Journal
FILE SEGMENT: PHYS; LIFE
LANGUAGE: English
REFERENCE COUNT: 27
ENTRY DATE: Entered STN: 1994
Last Updated on STN: 1994

L15 ANSWER 49 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 9

ACCESSION NUMBER: 1992:408467 CAPLUS Full-text
DOCUMENT NUMBER: 117:8467
TITLE: ACE-inhibitors [ACE = angiotensin converting enzyme] through the reaction of 4-hydroxy-2-butynoates with (S)-amino-acid esters: a structural study on N-[3-(4'-dimethylaminophenyl)-1-(S)-ethoxycarbonyl-3-oxoprop-1-yl]-(S)-alanine benzyl ester
AUTHOR(S): Arcadi, Antonio; Cacchi, Sandro; Marinelli, Fabio; Adovasio, Victor; Nardelli, Mario
CORPORATE SOURCE: Dip. Chim., Ing. Chim. Mater., Univ. Aquila, L'Aquila, I-67100, Italy
SOURCE: Gazzetta Chimica Italiana (1992), 122(3), 127-32 CODEN: GCITA9; ISSN: 0016-5603
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 117:8467
GI



I

AB The crystal and mol. structure of the title compound (I) has been determined by single crystal x-ray diffraction data collected using both Mo-Kα and Cu-Kα radiations. The results of the two analyses are in good agreement and confirm the NMR-based regiochem. of the conjugate addition step. The mol. has an extended conformation and the two asym. centers have the same S,S chirality. The conformation is discussed on the basis of the van der Waals-interactions.

L15 ANSWER 50 OF 65 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 91140595 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 1995891
TITLE: Configuration and preferential solid-state conformations of perindoprilat (S-9780). Comparison with the crystal structures of other ACE inhibitors and conclusions related to structure-activity relationships.
AUTHOR: Pascard C; Guilhem J; Vincent M; Remond G; Portevin B; Laubie M
CORPORATE SOURCE: Institut de Chimie des Substances Naturelles, Gif-sur-Yvette, France.
SOURCE: Journal of medicinal chemistry, (1991 Feb) Vol. 34, No. 2, pp. 663-9.
Journal code: 9716531. ISSN: 0022-2623.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199103
ENTRY DATE: Entered STN: 19910412
Last Updated on STN: 19910412
Entered Medline: 19910327

AB The conformation of perindoprilat, an antihypertensive drug, is studied in the solid state by X-ray analysis. The resolution of its structure reveals important analogies between its observed conformation and that of several ACE inhibitors of the same family. This comparison points out a constant relative orientation of the functional groups, regardless of the molecular environment. This angular constancy appears to us as not being accidental and is a good argument for the spatial design of the ACE binding site. Although ACE is a carboxydipeptidase, the binding site may not contain two but one unique hydrophobic pocket receiving the C-terminal end of the inhibitors.

L15 ANSWER 51 OF 65 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 91140570 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 1995872
TITLE: Molecular and crystal structures of MDL27,467A hydrochloride and quinapril hydrochloride, two ester derivatives of potent angiotensin converting enzyme inhibitors.
AUTHOR: Hausin R J; Codding P W
CORPORATE SOURCE: Department of Chemistry, University of Calgary, Alberta, Canada.
SOURCE: Journal of medicinal chemistry, (1991 Feb) Vol. 34, No. 2, pp. 511-7.
Journal code: 9716531. ISSN: 0022-2623.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199103
ENTRY DATE: Entered STN: 19910412
Last Updated on STN: 19910412
Entered Medline: 19910327

AB The molecular structures of MDL27,467A hydrochloride, [4 alpha,7 alpha(R*),12b beta]-7-[[1-(ethoxycarbonyl)-3-phenyl-propyl] amino]-1,2,3,4,6,7,12a,12b-octahydro-6-oxopyrido[2,1- a][2]benzazepine-4- carboxylic acid diphenylmethyl ester hydrochloride, and quinapril hydrochloride, [3S-[2[R*(R*)],3R]]-2-[2[[1- (ethoxycarbonyl)-3- phenylpropyl]-amino]-1-oxopropyl]-1,2,3,4- tetrahydro-3- isoquinolinecarboxylic acid hydrochloride, were determined by X- ray diffraction methods. The modified, C-terminal dipeptide portions and the phenylpropyl fragments in both crystal structures adopt similar conformations. The binding positions for several pharmacophores are defined by the constraint of the tricyclic system in the crystallographic structure of MDL27,467A hydrochloride. Conformational energy calculations show that the phenyl ring of the tetrahydro-3-isoquinoline system of quinapril does not fit into the S2 hydrophobic pocket of angiotensin converting enzyme.

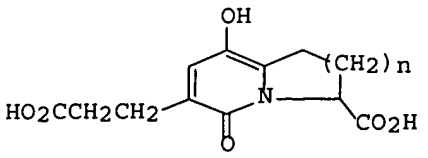
L15 ANSWER 52 OF 65 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN
ACCESSION NUMBER: 1991:605997 SCISEARCH Full-text
THE GENUINE ARTICLE: GM721

TITLE: INORGANIC-CHEMISTRY AND DRUG DESIGN
AUTHOR: SADLER P J (Reprint)
CORPORATE SOURCE: UNIV LONDON, BIRKBECK COLL, DEPT CHEM, LONDON WC1H 0PP, ENGLAND (Reprint)
COUNTRY OF AUTHOR: ENGLAND
SOURCE: ADVANCES IN INORGANIC CHEMISTRY, (1991) Vol. 36, pp. 1-48. ISSN: 0065-2792.
PUBLISHER: ACADEMIC PRESS INC JNL-COMP SUBSCRIPTIONS, 525 B ST, STE 1900, SAN DIEGO, CA 92101-4495.
DOCUMENT TYPE: General Review; Journal
LANGUAGE: English
REFERENCE COUNT: 150
ENTRY DATE: Entered STN: 1994
Last Updated on STN: 1994

L15 ANSWER 53 OF 65 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 90300488 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 2362274
TITLE: Crystallographic studies of angiotensin converting enzyme inhibitors and analysis of preferred zinc coordination geometry.
AUTHOR: Hausin R J; Codding P W
CORPORATE SOURCE: Department of Chemistry, University of Calgary, Alberta, Canada.
SOURCE: Journal of medicinal chemistry, (1990 Jul) Vol. 33, No. 7, pp. 1940-7.
Journal code: 9716531. ISSN: 0022-2623.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199008
ENTRY DATE: Entered STN: 19900907
Last Updated on STN: 19970203
Entered Medline: 19900806

AB The molecular structures of two potent inhibitors of angiotensin converting enzyme (ACE, EC 3.4.15.1, dipeptidyl carboxypeptidase), ketoace, (5S)-5-benzamido-4-oxo-6-phenylhexanoyl-L-proline, and (1S,2R)-1-[[2-(benzoylthio)- cyclopentyl]carbonyl]-L-proline were determined by X-ray diffraction methods. The distances between the binding functions in both crystal structures are in agreement with the experimental results for the hypertension drug captopril and the enzyme substrate hippuryl-L-histidyl-L-leucine. The modified peptide skeletons of both inhibitors adopt extended conformations with the proline amide bond trans. Crystallographic data have been used to determine the coordination geometry for zinc-sulfhydryl and zinc-carbonyl interactions. Coordination distances and bond angles are found to be different from values assumed in models of the angiotensin converting enzyme active site. No preferred torsion angles for a zinc-sulfhydryl inhibitor interaction can be identified. Superposition of the crystallographic structures of four ACE ligands shows that the observed extended conformations place the pharmacophores, zinc atom ligand, carbonyl oxygen atom, and carboxyl group, in juxtaposition and provide an alternative model for the interaction of ligands with the ACE active site.

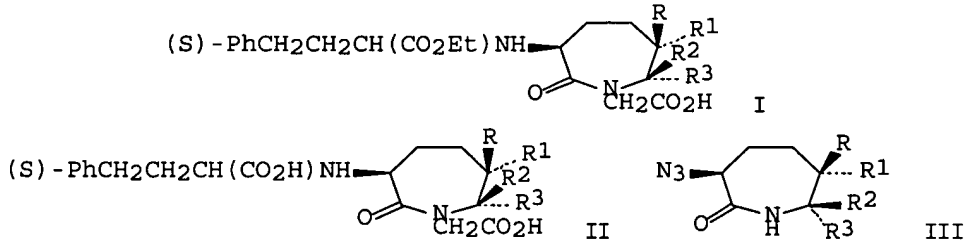
L15 ANSWER 54 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:528673 CAPLUS Full-text
DOCUMENT NUMBER: 109:128673
TITLE: Structure elucidation of A58365A and A58365B, angiotensin converting enzyme inhibitors produced by Streptomyces chromofuscus
AUTHOR(S): Hunt, Ann H.; Mynderse, Jon S.; Samlaska, Susan K.; Fukuda, David S.; Maciak, George M.; Kirst, Herbert A.; Occolowitz, John L.; Swartzendruber, John K.; Jones, Noel D.
CORPORATE SOURCE: Lilly Res. Lab., Eli Lilly and Co., Indianapolis, IN, 46285, USA
SOURCE: Journal of Antibiotics (1988), 41(6), 771-9
CODEN: JANTAJ; ISSN: 0021-8820
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



I, n=1
II, n=2

AB The structure formulas of A58365A (I) and A58365B (II) angiotensin converting enzyme inhibitors, isolated from the culture filtrate of S. chromofuscus NRRC 15098, were established by 1H-NMR and 13C-NMR and UV spectra. Catalytic hydrogenation of I gave a tetrahydrodeoxy derivative Extensive decoupling studies by using 1H NMR spectrometry at 360 MH3 allowed all nonexchangeable proton of the derivative to be connected in a continuous substructure. The structure was confirmed by an independent x-ray anal. of the di-Me ester of I.

L15 ANSWER 55 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:55878 CAPLUS Full-text
DOCUMENT NUMBER: 108:55878
TITLE: **Angiotensin-converting enzyme inhibitors. 2. Perhydroazepin-2-one derivatives**
AUTHOR(S): Yanagisawa, Hiroaki; Ishihara, Sadao; Ando, Akiko; Kanazaki, Takuro; Miyamoto, Shuichi; Koike, Hiroyuki; Iijima, Yasuteru; Oizumi, Kiyoshi; Matsushita, Yoichi; Hata, Tadashi
CORPORATE SOURCE: Chem. Res. Lab., Sankyo Co., Ltd., Tokyo, 140, Japan
SOURCE: Journal of Medicinal Chemistry (1988), 31(2), 422-8
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 108:55878
GI



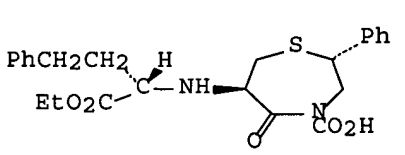
AB Chiral [[(carbethoxyphenylpropyl)amino]oxophenylperhydroazepino]acetic acids I (R = Ph, R1-R3 = H; R1 = Ph, R = R2 = R3 = H; R2 = Ph, R = R1 = R3 = H; R3 = Ph, R-R2 = H) and diacids II (same R-R3) were prepared and evaluated for angiotensin-converting enzyme inhibition. II (R or R1 or R2 = Ph) showed in vivo inhibition greater than that of enalaprilat. I (R or R1 or R2 = Ph), p.o. in rats, suppressed the pressor response to angiotensin I administered i.v. The structure-activity relationships of I and II were discussed based on MNDO calcns. of their conformations. The structures of azidoperhydroazepinones III (R = Ph, R1-R3 = H; R1 = Ph, R = R2 = R3 = H; R2 = Ph, R = R1 = R3 = H) were determined by x-ray crystallog.

L15 ANSWER 56 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 13
ACCESSION NUMBER: 1988:488769 CAPLUS Full-text

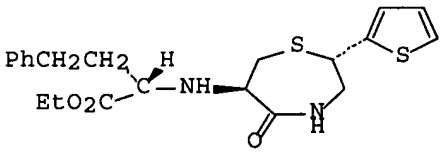
DOCUMENT NUMBER: 109:88769
TITLE: Molecular modeling of the active site of enkephalin-degrading neutral endopeptidase-24.11 (enkephalinase). An active site model for neutral endopeptidase-24.11
AUTHOR(S): Andrews, Peter R.; Iskander, Magdy N.; Issa, John; Reiss, James A.
CORPORATE SOURCE: Sch. Pharm. Chem., Victorian Coll. Pharm. Ltd., Parkville, 3052, Australia
SOURCE: Quantitative Structure-Activity Relationships (1988), 7(1), 1-6
CODEN: QSARDI; ISSN: 0722-3676
DOCUMENT TYPE: Journal
LANGUAGE: English

AB The active site regions of thermolysin (TLN) and carboxypeptidase A (CPA) are directly compared by superimposition of the published crystal structures of 8 TLN-inhibitor complexes and 4 CPA-inhibitor complexes. There is a remarkable similarity in the S'1 region of these 2 Zn metalloenzymes, and it is suggested that this may be a common feature among other enzymes of this class, including the enkephalin-degrading neutral endopeptidase of enkephalinase (NEP-24.11). Assuming this common feature, the possible geometry of the S'2 region of enkephalinase was determined by performing classical potential energy calcns. on potent NEP-24.11 inhibitors. The active conformation of these inhibitors was thus identified as similar to that found in the x-ray crystal structure of TLN-inhibitor complexes. It is proposed that the active site region of TLN should serve as a reasonable model for that of NEP-24.11. Extension of the model to the case of angiotensin -converting enzyme (ACE) showed that this enzyme might have a similar S'1 region to the other 3 enzymes and allowed further definition of the ACE model previously developed.

L15 ANSWER 57 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1988:37803 CAPLUS Full-text
DOCUMENT NUMBER: 108:37803
TITLE: Angiotensin-converting enzyme inhibitors. Perhydro-1,4-thiazepin-5-one derivatives
AUTHOR(S): Yanagisawa, Hiroaki; Ishihara, Sadao; Ando, Akiko; Kanazaki, Takuro; Miyamoto, Shuichi; Koike, Hiroyuki; Iijima, Yasuteru; Oizumi, Kiyoshi; Matsushita, Yoichi; Hata, Tadashi
CORPORATE SOURCE: Chem. Res. Lab., Sankyo Co., Ltd., Tokyo, 140, Japan
SOURCE: Journal of Medicinal Chemistry (1987), 30(11), 1984-91
CODEN: JMCMAR; ISSN: 0022-2623
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 108:37803
GI



I



II

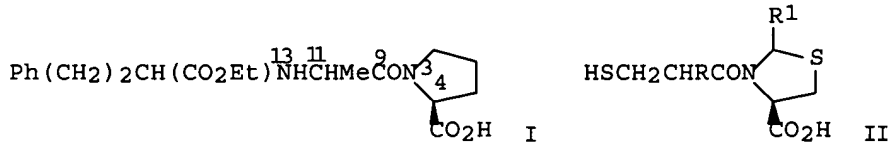
AB Aminooxoperhydrothiazepinylacetic acids, e.g. I, (monoester monoacids) and their dicarboxylic acids containing hydrophobic Ph or thienyl substituents at the 2- or 3-position of the thiazepinone ring were prepared and assayed for angiotensin-converting enzyme (ACE) inhibitory activity. The dicarboxylic acids having the pseudoequatorial amino groups at the 6-position and the pseudoequatorial hydrophobic substituents at the 2- or 3-position of the chair conformation of the thiazepinone ring had potent in vitro inhibitory activity. The monoester monoacids having the hydrophobic substituents at the 2-position suppressed pressor response to angiotensin I for a longer duration than those having the substituents at the 3-position when administered orally. The structure-activity relationship was studied by conformational energy calcns. of the thiazepinone

ring. The x-ray crystal structure of 2-thienylperhydrothiazepinone II, an intermediate in the preparation of the N-carboxylated derivative, was determined

L15 ANSWER 58 OF 65 MEDLINE on STN DUPLICATE 14
ACCESSION NUMBER: 87229021 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 3295561
TITLE: High resolution X-ray analyses of renin inhibitor-aspartic proteinase complexes.
AUTHOR: Foundling S I; Cooper J; Watson F E; Cleasby A; Pearl L H; Sibanda B L; Hemmings A; Wood S P; Blundell T L; Valler M J; +
SOURCE: Nature, (1987 May 28-Jun 3) Vol. 327, No. 6120, pp. 349-52. Journal code: 0410462. ISSN: 0028-0836.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198707
ENTRY DATE: Entered STN: 19900305
Last Updated on STN: 20000303
Entered Medline: 19870702

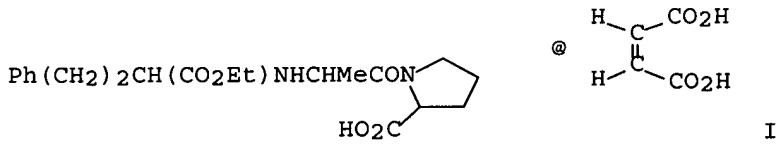
AB Inhibitors of the conversion of angiotensinogen to the vasoconstrictor angiotensin II have considerable value as antihypertensive agents. For example, captopril and enalapril are clinically useful as inhibitors of angiotensin-converting enzyme. This has encouraged intense activity in the development of inhibitors of kidney renin, which is a very specific aspartic proteinase catalysing the first and rate limiting step in the conversion of angiotensinogen to angiotensin II. The most effective inhibitors such as H-142 and L-363,564 have used non-hydrolysable analogues of the proposed transition state, and partial sequences of angiotensinogen (Table 1). H-142 is effective in lowering blood pressure in humans but has no significant effect on other aspartic proteinases such as pepsin in the human body (Table 1). At present there are no crystal structures available for human or mouse renins although three-dimensional models demonstrate close structural similarity to other spartic proteinases. We have therefore determined by X -ray analysis the three-dimensional structures of H-142 and L-363,564 complexed with the aspartic proteinase endothiapepsin, which binds these inhibitors with affinities not greatly different from those measured against human renin (Table 1). The structures of these complexes and of that between endothiapepsin and the general aspartic proteinase inhibitor, H-256 (Table 1) define the common hydrogen bonding schemes that allow subtle differences in side-chain orientations and in the positions of the transition state analogues with respect to the active-site aspartates.

L15 ANSWER 59 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 15
ACCESSION NUMBER: 1986:552979 CAPLUS Full-text
DOCUMENT NUMBER: 105:152979
TITLE: Conformational similarities of angiotensin-converting enzyme inhibitors: x-ray crystal structures
AUTHOR(S): In, Yasuko; Shibata, Megumi; Doi, Mitsunobu; Ishida, Toshimasa; Inoue, Masatoshi; Sasaki, Yasuto; Morimoto, Shiro
CORPORATE SOURCE: Osaka Coll. Pharm., Osaka, 580, Japan
SOURCE: Journal of the Chemical Society, Chemical Communications (1986), (6), 473-4
CODEN: JCCCAT; ISSN: 0022-4936
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB The structures of enalapril (MK 421) (I) and the thio analogs YS 980 (II; R = Me, R1 = H) and SA 446 (II; R = H, R1 = 2-HOC6H4), potent angiotensin-converting enzyme inhibitors, were determined by x-ray crystallog. anal. All 3 possess a common conformation with a trans zigzag geometry of the C(4)-N(3)-C(9)-C(11)-C(13)[N(13)] bond sequence and a cis orientation between the carboxy and amido carbonyl groups.

L15 ANSWER 60 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1986:193011 CAPLUS Full-text
DOCUMENT NUMBER: 104:193011
TITLE: High resolution spectroscopic evidence and solution calorimetry studies on the polymorphs of enalapril maleate
AUTHOR(S): Ip, Dominic P.; Brenner, Gerald S.; Stevenson, James M.; Lindenbaum, Siegfried; Douglas, Alan W.; Klein, S. David; McCauley, James A.
CORPORATE SOURCE: Merck Sharp and Dohme Res. Lab., West Point, PA, 19486, USA
SOURCE: International Journal of Pharmaceutics (1986), 28(2-3), 183-91
CODEN: IJPHDE; ISSN: 0378-5173
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



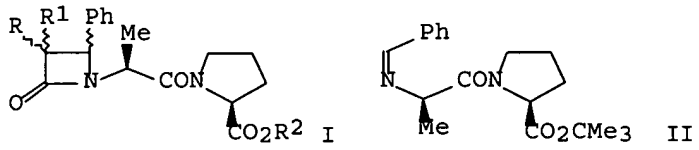
I

AB Enalapril maleate (I) [76095-16-4], a potent angiotensin- converting enzyme inhibitor, exists as polymorphs form I and form II. X-ray powder diffraction measurements have shown slightly different patterns. Differential scanning calorimetric thermograms failed to show any significant differences during melting. High resolution spectroscopic techniques, including solid state C-13 NMR, Fourier-transform IR and Raman, detect differences between form I and form II. Heats of solution data obtained also indicate measurable energy differences. Apparently, these 3 polymorphic forms of I are energetically very similar. Virtual equivalence of in vitro dissoln. rate was obtained from formulations of I made from either form I, or form II, or mixts.

L15 ANSWER 61 OF 65 MEDLINE on STN DUPLICATE 16
ACCESSION NUMBER: 84280080 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 6087816
TITLE: Azapeptides: a new class of angiotensin-converting enzyme inhibitors.
AUTHOR: Greenlee W J; Thorsett E D; Springer J P; Patchett A A; Ulm E H; Vassil T C
SOURCE: Biochemical and biophysical research communications, (1984 Jul 31) Vol. 122, No. 2, pp. 791-7.
Journal code: 0372516. ISSN: 0006-291X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 198409
ENTRY DATE: Entered STN: 19900320
Last Updated on STN: 19900320
Entered Medline: 19840912
AB A class of potent inhibitors of angiotensin-converting enzyme (dipeptidyl carboxypeptidase, E.C. 3.4.15.1) is reported, in which an alpha-aza substitution into the

substituted N-carboxymethyl dipeptide structure of enalapril is made. The inhibitors 2 exhibit striking alterations in their conformational and acid-base properties due to the aza substitution, as is clear from pKa data and the x- ray crystal structure of a model azapeptide. In spite of this, they bind tightly to the enzyme, with inhibitor potency comparable to that of captopril.

L15 ANSWER 62 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1984:192245 CAPLUS Full-text
DOCUMENT NUMBER: 100:192245
TITLE: The synthesis of peptide β-lactams as potential protease inhibitors
AUTHOR(S): Wharton, Clifford J.; Wrigglesworth, Roger; Rowe, Michael
CORPORATE SOURCE: Dep. Med. Chem., Wellcome Res. Lab., Beckenham, BR3 3BS, UK
SOURCE: Journal of the Chemical Society, Perkin Transactions 1: Organic and Bio-Organic Chemistry (1972-1999) (1984), (1), 29-39
CODEN: JCPRB4; ISSN: 0300-922X
DOCUMENT TYPE: Journal
LANGUAGE: English
GI



AB Mixts. of cis peptide β-lactams I (R = PhO, PhCH2O, HO, Cl, Br, R1 = H; R = PhSe, R1 = Me; R2 = CMe3, H) were prepared through cycloaddn. of imine II with RCHR1COCl. I are as potential inhibitors of angiotensin-converting enzyme. The absolute configurations of I were determined by NMR studies including nuclear Overhauser effect studies, and by x-ray crystallog. anal. of I (R = β-PhO, R1 = α-H, R2 = CMe3; α-Ph).

L15 ANSWER 63 OF 65 MEDLINE on STN DUPLICATE 17
ACCESSION NUMBER: 83125670 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 6297413
TITLE: Widespread foreign-body granulomas and elevated serum angiotensin-converting enzyme.
AUTHOR: Pucevich M V; Rosenberg E W; Bale G F; Terzakis J A
SOURCE: Archives of dermatology, (1983 Mar) Vol. 119, No. 3, pp. 229-34.
Journal code: 0372433. ISSN: 0003-987X.
PUB. COUNTRY: United States
DOCUMENT TYPE: (CASE REPORTS)
Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 198303
ENTRY DATE: Entered STN: 19900318
Last Updated on STN: 19900318
Entered Medline: 19830324

AB A patient had extensive foreign-body granulomatous inflammation of multiple skin sites and of the inguinal lymph nodes with splenomegaly, cutaneous anergy to common skin antigens, and peripheral blood eosinophilia. The patient had an elevated serum angiotensin-converting enzyme level. Histologically, the granulomas were of the foreign-body type with lymphocytes, histiocytes, eosinophils, and giant cells, some that contained doubly refractile crystalline material. Electron-probe x-ray microanalysis identified silicon, magnesium, iron, calcium, phosphorus, zinc, titanium, and chromium in the crystalline material. These findings suggest talc, cement, and inorganic pigment as possible sources

of the crystals . This case is reported for its unusual clinical, laboratory, and morphologic features.

L15 ANSWER 64 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 18
ACCESSION NUMBER: 1982:472278 CAPLUS Full-text
DOCUMENT NUMBER: 97:72278
TITLE: Thiol compounds. V. Absolute configuration and crystal structure of (4R)-2-(2-hydroxyphenyl)-3-(3-mercaptopropionyl)-4-thiazolidinecarboxylic acid
AUTHOR(S): Oya, Masayuki; Kato, Eishin; Iwao, Junichi; Yasuoka, Noritake
CORPORATE SOURCE: Res. Lab., Santen Pharm. Co., Ltd., Osaka, 533, Japan
SOURCE: Chemical & Pharmaceutical Bulletin (1982), 30(2), 484-93
CODEN: CPBTAL; ISSN: 0009-2363
DOCUMENT TYPE: Journal
LANGUAGE: English
OTHER SOURCE(S): CASREACT 97:72278
AB The absolute configuration of (1R)-2-(2-hydroxyphenyl)-3-(3-mercaptopropionyl)- 4-thiazolidinecarboxylic acid, SA 446, which has a potent inhibitory activity against angiotensin I-converting enzyme (ACE), was determined to be (2R,4R) by NMR spectroscopy, sp. rotation measurement and x-ray crystallog. The structure-activity relationships of the (2R,4R)- and (2S,4R)-isomers are discussed, and stereoselective acylation of (4R)-2-aryl-4-thiazolidinecarboxylic acids is also described.

L15 ANSWER 65 OF 65 CAPLUS COPYRIGHT 2006 ACS on STN
ACCESSION NUMBER: 1970:439681 CAPLUS Full-text
DOCUMENT NUMBER: 73:39681
TITLE: Crystal and molecular structure of 5α-acetoxy-6β-bromohexahydrophysalin A
AUTHOR(S): Kawai, Mitsuru; Matsuura, Teruo; Taga, T.; Osaki, Kenji
CORPORATE SOURCE: Fac. Eng., Kyoto Univ., Kyoto, Japan
SOURCE: Journal of the Chemical Society [Section] B: Physical Organic (1970), (5), 812-15
CODEN: JCSPAC; ISSN: 0045-6470
DOCUMENT TYPE: Journal
LANGUAGE: English
AB 5α-Ace, toxy-6β-bromohexahydrophysalin A has a novel 13,14-seco-16,24-cyclo-C28-steroidal structure by x-ray crystal structure anal. The crystals are monoclinic, space group P21, with 2 mols. of C30H37O12Br.2CH4O in the unit cell of dimensions a 24.09 ± 0.05, b 7.60 ± 0.02, c 8.74 ± 0.03 Å, and β = 96.0° ± 0.2°. The crystal structure was elucidated by the heavy-atom method, and the atomic coordinates were refined by Fourier and least-squares calcns. The final R value over 3716 independent reflections is 0.105. The absolute configuration was determined by the anomalous dispersion method.

=> s (angiotensin converting enzyme-2 or ACE-2) and crystal and x-ray
L16 1 FILE MEDLINE
L17 1 FILE CAPLUS
L18 2 FILE SCISEARCH
L19 0 FILE LIFESCI
L20 0 FILE BIOSIS
L21 0 FILE EMBASE

TOTAL FOR ALL FILES
L22 4 (ANGIOTENSIN CONVERTING ENZYME-2 OR ACE-2) AND CRYSTAL AND X-RAY

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PROCESSING COMPLETED FOR L22
L23 3 DUP REM L22 (1 DUPLICATE REMOVED)

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L23 ANSWER 1 OF 3 MEDLINE on STN
ACCESSION NUMBER: 2005495389 MEDLINE Full-text
DOCUMENT NUMBER: PubMed ID: 16166518
TITLE: Structure of SARS coronavirus spike receptor-binding domain complexed with receptor.
AUTHOR: Li Fang; Li Wenhui; Farzan Michael; Harrison Stephen C

CORPORATE SOURCE: Department of Biological Chemistry and Molecular Pharmacology, Harvard Medical School and Laboratory of Molecular Medicine, 320 Longwood Avenue, Boston, MA 02115, USA.
CONTRACT NUMBER: AI061601 (NIAID)
CA13202 (NCI)
SOURCE: Science, (2005 Sep 16) Vol. 309, No. 5742, pp. 1864-8.
Journal code: 0404511. E-ISSN: 1095-9203.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
OTHER SOURCE: PDB-2AJF
ENTRY MONTH: 200509
ENTRY DATE: Entered STN: 20050917
Last Updated on STN: 20050929
Entered Medline: 20050928

AB The spike protein (S) of SARS coronavirus (SARS-CoV) attaches the virus to its cellular receptor, angiotensin-converting enzyme 2 (ACE2). A defined receptor-binding domain (RBD) on S mediates this interaction. The crystal structure at 2.9 angstrom resolution of the RBD bound with the peptidase domain of human ACE2 shows that the RBD presents a gently concave surface, which cradles the N-terminal lobe of the peptidase. The atomic details at the interface between the two proteins clarify the importance of residue changes that facilitate efficient cross-species infection and human-to-human transmission. The structure of the RBD suggests ways to make truncated disulfide-stabilized RBD variants for use in the design of coronavirus vaccines.

=> d ibib abs 2-3

L23 ANSWER 2 OF 3 CAPLUS COPYRIGHT 2006 ACS on STN DUPLICATE 1
ACCESSION NUMBER: 2005:1256205 CAPLUS Full-text
DOCUMENT NUMBER: 144:100959
TITLE: Orally active antioxidative copper(II) aspirinate: synthesis, structure characterization, superoxide scavenging activity, and in vitro and in vivo antioxidative evaluations
AUTHOR(S): Fujimori, T.; Yamada, S.; Yasui, H.; Sakurai, H.; In, Y.; Ishida, T.
CORPORATE SOURCE: Department of Analytical and Bioinorganic Chemistry, Kyoto Pharmaceutical University, 5 Nacauchi-cho, Misasagi, Yamashina-ku, Kyoto, 607-8414, Japan
SOURCE: JBIC, Journal of Biological Inorganic Chemistry (2005), 10(8), 831-841
CODEN: JJBCFA; ISSN: 0949-8257
PUBLISHER: Springer GmbH
DOCUMENT TYPE: Journal
LANGUAGE: English

AB Ever since it was proposed that reactive oxygen species (ROS) are involved in the pathogenesis of various diseases, superoxide dismutase (SOD)-mimetic complexes have been intensively studied. The authors prepared copper(II) aspirinate [Cu2(asp)4] from Cu(II) and aspirin, which has been in use for many years as an antipyretic, an analgesic, and an anti-inflammatory agent. However, Cu2(asp)4 has been found to have addnl. activities, including anti-inflammatory, antiulcer, anti- ischemic/reperfusion agent, anticancer, antimutagenic, and antimicrobial activities. The activity of copper salicylate [Cu(sal)2] was also compared with that of Cu2(asp)4. The structure of the Cu2(asp)4 was determined using x-ray structure anal. Its SOD-mimetic activity was determined using cytochrome c, ESR spectroscopy, and ESR spin trap methods. The activity of Cu2(asp)4 was slightly greater than CuSO4 and copper acetate [Cu(ace)2] and slightly less than that of Cu(sal)2. The in vitro antioxidant activity, evaluated in human epithelial or transformed neoplastic keratinocyte cells, HaCaT, and normal dermal fibroblasts in terms of cell survival following UV B (UVB) irradiation, was significantly increased in the presence of Cu2(asp)4, Cu(sal)2, and CuSO4. Further, ROS generation following UVA irradiation in the skin of hairless mice following oral treatment with Cu2(asp)4 for three consecutive days was significantly suppressed compared to the vehicle- or Cu(ace)2-treated mice. On the basis of these results, Cu2(asp)4 was observed to be a potent antioxidative compound possessing antioxidative activity in biol. systems. In conclusion, Cu2(asp)4 is a potent antioxidative agent that may be useful for future treatment of diseases resulting from ROS.

REFERENCE COUNT: 38 THERE ARE 38 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L23 ANSWER 3 OF 3 SCISEARCH COPYRIGHT (c) 2006 The Thomson Corporation on STN

ACCESSION NUMBER: 2004:997366 SCISEARCH Full-text

THE GENUINE ARTICLE: 866SR

TITLE: Immunological, structural, and preliminary X-ray diffraction characterizations of the fusion core of the SARS-coronavirus spike protein

AUTHOR: Hsu C H; Ko T P; Yu H M; Tang T K; Chen S T; Wang A H J (Reprint)

CORPORATE SOURCE: Acad Sinica, Inst Biol Chem, Taipei 115, Taiwan (Reprint)
ahwang@gate.sinica.edu.tw

COUNTRY OF AUTHOR: Taiwan

SOURCE: BIOCHEMICAL AND BIOPHYSICAL RESEARCH COMMUNICATIONS, (12 NOV 2004) Vol. 324, No. 2, pp. 761-767.
ISSN: 0006-291X.

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DOCUMENT TYPE: Article; Journal

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ABSTRACT IS AVAILABLE IN THE ALL AND IALL FORMATS

AB The SARS-CoV spike protein, a glycoprotein essential for viral entry, is a primary target for vaccine and drug development. Two peptides denoted HR-N(SN50) and HR-C(SC40), corresponding to the Leu/Ile/Val-rich heptad-repeat regions from the N-terminal and C-terminal segments of the SARS-CoV spike S2 sequence, respectively, were synthesized and predicted to form trimeric assembly of hairpin-like structures. The polyclonal antibodies produced by recombinant S2 protein were tested for antigenicity of the two heptad repeats. We report here the first crystallographic study of the SARS spike HR-N/HR-C complex. The crystal belongs to the triclinic space group P1 and the data-set collected to 2.98 Angstrom resolution showed noncrystallographic pseudo-222 and 3-fold symmetries. Based on these data, comparative modeling of the SARS-CoV fusion core was performed. The immunological and structural information presented herein may provide a more detailed understanding of the viral fusion mechanism as well as the development of effective therapy against SARS-CoV infection. (C) 2004 Elsevier Inc. All rights reserved.

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WEST Search History

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DATE: Tuesday, April 11, 2006

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		DB=PGPB; THES=ASSIGNEE; PLUR=YES; OP=ADJ	
☐	L11	angiotensin adj3 converting enzyme adj3 related carboxypeptidse or angiotensin adj3 converting enzyme adj3 2	20
		DB=USPT,USOC,EPAB,JPAB,DWPI; THES=ASSIGNEE; PLUR=YES; OP=ADJ	
☐	L10	angiotensin adj3 converting enzyme adj3 related carboxypeptidse or angiotensin adj3 converting enzyme adj3 2	52
☐	L9	L8 and atomic coordinate	1
☐	L8	(angiotensin adj3 converting enzyme adj3 related carboxypeptidse or angiotensin adj3 converting enzyme adj3 2 or ACE adj3 2) and crystal and x-ray	102
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☐	L7	L6 and atomic coordinate	4
☐	L6	(angiotensin adj3 converting enzyme adj3 related carboxypeptidse or angiotensin adj3 converting enzyme adj3 2 or ACE adj3 2) and crystal and x-ray	395
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☐	L4	(angiotensin adj3 converting enzyme adj3 related carboxypeptidse or angiotensin adj3 converting enzyme adj3 2 or ACE adj3 2) same crystal and x-ray	3
		DB=USPT,USOC,EPAB,JPAB,DWPI; THES=ASSIGNEE; PLUR=YES; OP=ADJ	
☐	L3	(angiotensin adj3 converting enzyme adj3 related carboxypeptidse or angiotensin adj3 converting enzyme adj3 2 or ACE adj3 2) same crystal and x-ray	5
☐	L2	(angiotensin adj3 converting enzyme adj3 related carboxypeptidse or angiotensin adj3 converting enzyme adj3 2 or ACE adj3 2) same crystal	85
☐	L1	(angiotensin adj3 converting enzyme adj3 related carboxypeptidse or angiotensin adj3 converting enzyme adj3 2 or ACE adj3 2)	5458

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Search Results - Record(s) 1 through 30 of 52 returned.

☐ 1. Document ID: US 6989363 B1

Using default format because multiple data bases are involved.

L10: Entry 1 of 52 File: USPT Jan 24, 2006

US-PAT-NO: 6989363
DOCUMENT-IDENTIFIER: US 6989363 B1

TITLE: Angiotensin converting enzyme homolog and therapeutic and diagnostic uses therefor

DATE-ISSUED: January 24, 2006

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Acton; Susan L.	Lexington	MA		US
Robison; Keith Earl	Wilmington	MA		US
Hsieh; Frank Y.	Lexington	MA		US

US-CL-CURRENT: 514/2; 530/316, 530/350

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 2. Document ID: US 6960683 B2

L10: Entry 2 of 52 File: USPT Nov 1, 2005

US-PAT-NO: 6960683
DOCUMENT-IDENTIFIER: US 6960683 B2

TITLE: Salt forms of poorly soluble probucol esters and ethers

DATE-ISSUED: November 1, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Meng; Charles Q.	Alpharetta	GA		

US-CL-CURRENT: 562/427; 564/503, 568/784

ABSTRACT:

Organic amine salts of compounds of the formula: ##STR1##

and their pharmaceutically acceptable salts, and uses in medical therapy are provided.

59 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 3. Document ID: US 6911459 B2

L10: Entry 3 of 52 File: USPT Jun 28, 2005

US-PAT-NO: 6911459
DOCUMENT-IDENTIFIER: US 6911459 B2

TITLE: Pharmaceutical composition

DATE-ISSUED: June 28, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ikeda; Hitoshi	Higashiosaka			JP
Sohda; Takashi	Takatsuki			JP
Odaka; Hiroyuki	Kobe			JP

US-CL-CURRENT: 514/342; 514/340, 514/369, 514/376, 546/269.7, 546/271.4, 548/183, 548/227

ABSTRACT:

Pharmaceutical composition which comprises an insulin sensitivity enhancer in combination with other antidiabetics differing from the enhancer in the mechanism of action, which shows a potent depressive effect on diabetic hyperglycemia and is useful for prophylaxis and treatment of diabetes.

15 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 4. Document ID: US 6902888 B1

L10: Entry 4 of 52 File: USPT Jun 7, 2005

US-PAT-NO: 6902888
DOCUMENT-IDENTIFIER: US 6902888 B1

TITLE: Diabetes gene

DATE-ISSUED: June 7, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
McGrail; Maura	Salt Lake City	UT		
Russell; Deanna L.	Salt Lake City	UT		
Shattuck; Donna M.	Salt Lake City	UT		

US-CL-CURRENT: 435/6; 435/91.1, 536/23.1, 536/23.5, 536/24.31

ABSTRACT:

The present invention relates generally to the field of human genetics. Specifically, the present invention relates to methods and materials used to isolate and detect human diabetes mellitus predisposing gene, specifically the angiotensinogen (AGT) gene, some mutant alleles of which cause susceptibility to insulin-dependent diabetes mellitus (IDDM). More specifically, the invention relates to gernline mutations in the AGT gene and their use in the diagnosis of predisposition to diabetes. The invention also relates to the prophylaxis and/or therapy of diabetes associated with a mutation in the AGT gene. The invention further relates to the screening of drugs for diabetes therapy. Finally, the invention relates to the screening of the AGT gene for mutations, which are useful for diagnosing the predisposition to diabetes.

7 Claims, 3 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 3

☐ 5. Document ID: US 6900033 B2

L10: Entry 5 of 52 File: USPT May 31, 2005

US-PAT-NO: 6900033
DOCUMENT-IDENTIFIER: US 6900033 B2
**** See image for Certificate of Correction ****

TITLE: Methods and compositions for modulating ACE-2 activity

DATE-ISSUED: May 31, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Parry; Tom J.	Walkersville	MD		
Sekut; Les	Ijamsville	MD		
Rosen; Craig A.	Laytonsville	MD		
Albert; Vivian R.	Rockville	MD		
Sanyal; Indrajit	Bethesda	MD		
Huang; Lili	Burlington	MA		
Wescott; Charles R.	Belmont	MA		

US-CL-CURRENT: 435/69.1; 435/226, 435/320.1, 435/325, 514/12, 530/324

ABSTRACT:

Binding polypeptides comprising specific amino acid sequences are disclosed that specifically bind ACE-2 protein or ACE-2-like polypeptides. The binding polypeptides can be used in methods of the invention for detecting, isolating, or purifying ACE-2 protein or ACE-2-like polypeptides in solutions or mixtures, or biological samples. The invention also relates to nucleic acid molecules encoding these ACE-2 binding polypeptides, vectors and host cells containing these nucleic acids, and methods for producing the same. The present invention also relates to methods and compositions for detecting, diagnosing, prognosing, preventing, treating or ameliorating a disease or disorder associated with aberrant ACE-2 or ACE-2 receptor expression or inappropriate function of ACE-2 or ACE-2 receptor, comprising use of ACE-2 binding polypeptides or fragments or variants thereof, that specifically bind to ACE-2.

11 Claims, 4 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 4

☐ 6. Document ID: US 6884771 B1

L10: Entry 6 of 52 File: USPT Apr 26, 2005

US-PAT-NO: 6884771
DOCUMENT-IDENTIFIER: US 6884771 B1

TITLE: Angiotensin converting enzyme homolog and uses therefor

DATE-ISSUED: April 26, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Acton; Susan	Lexington	MA		
Robison; Keith E.	Wilmington	MA		
Hsieh; Frank Y.	Lexington	MA		

US-CL-CURRENT: 514/2; 424/94.1, 424/94.6, 435/183, 435/195, 514/12, 530/350, 530/361

ABSTRACT:

The present invention relates to the discovery of novel genes encoding an angiotensin converting enzyme, Angiotensin Converting Enzyme-2 (ACE-2). The invention provides therapeutics, prognostic and diagnostics methods for treating blood pressure related disorders as well as various types of allergic conditions, among others. Also disclosed are screening assays for identifying compounds for treating and preventing these conditions.

25 Claims, 27 Drawing figures

Exemplary Claim Number: 1
Number of Drawing Sheets: 23

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 7. Document ID: US 6770741 B1

L10: Entry 7 of 52 File: USPT Aug 3, 2004

US-PAT-NO: 6770741
DOCUMENT-IDENTIFIER: US 6770741 B1

TITLE: Brandykinin antagonist peptides

DATE-ISSUED: August 3, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kyle; Donald James	Abingdon	MD		
Hiner; Roger Neal	Baltimore	MD		

US-CL-CURRENT: 530/314; 530/328, 530/332

ABSTRACT:

The substitution of the L-Pro at the 7-position of the peptide hormone bradykinin or other substituted analogs of bradykinin with a D-configuration hydroxyproline ether or thioether converts bradykinin agonists into bradykinin antagonists. The invention further includes the intermediate compounds and additional modifications at other positions within the novel 7-position modified bradykinin antagonists which increase enzyme resistance, antagonist potency, and/or specificity of the new bradykinin antagonists. The analogs produced are useful in treating conditions and diseases of a mammal and human in which an excess of bradykinin or related kinins are produced or injected such as by insect bites.

4 Claims, 3 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 8. Document ID: US 6716852 B2

L10: Entry 8 of 52 File: USPT Apr 6, 2004

US-PAT-NO: 6716852
DOCUMENT-IDENTIFIER: US 6716852 B2

TITLE: Amino acid derivatives and use thereof as NEP, ACE and ECE inhibitors

DATE-ISSUED: April 6, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Roques; Bernard P.	Paris			FR
Fournie-Zaluski; Marie-Claude	Paris			FR
Inguimbert; Nicolas	Cachan			FR
Poras; Herve	Alfortville			FR
Scalbert; Elizabeth	Paris			FR
Bennejean; Caroline	Charenton le Pont			FR
Renard; Pierre	Le Chesnay			FR

US-CL-CURRENT: 514/292; 514/300, 514/419, 546/113, 546/84, 548/496

ABSTRACT:

The invention relates to compounds of formula (I): ##STR1##

wherein 0.ltoreq.n.ltoreq.3, 0.ltoreq.m.ltoreq.6, R.sup.3 and R.sup.4 together form phenyl, B represents heteroaryl, R.sup.1 and R.sup.2 represent hydrogen or groups as defined in the description.

and medicinal products containing the same which are useful in treating or preventing arterial hypertension and cardiovascular diseases.

26 Claims, 0 Drawing figures
Exemplary Claim Number: 1

☐ 9. Document ID: US 6699869 B1

L10: Entry 9 of 52 File: USPT Mar 2, 2004

US-PAT-NO: 6699869
DOCUMENT-IDENTIFIER: US 6699869 B1

TITLE: .beta.-sheet mimetics and use thereof as inhibitors of biologically active peptides or proteins

DATE-ISSUED: March 2, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kahn; Michael	Kirkland	WA		
Ogbu; Cyprian O.	Bellevue	WA		
Eguchi; Masakatsu	Bellevue	WA		
Kim; Hwa-Ok	Redmond	WA		
Boatman, Jr.; Patrick Douglas	Issaquah	WA		

US-CL-CURRENT: 514/248; 514/221, 514/405, 548/356.1, 562/562

ABSTRACT:

There are disclosed .beta.-sheet mimetics and methods relating to the same for imparting or stabilizing the .beta.-sheet structure of a peptide, protein or molecule. In one aspect, .beta.-sheet mimetics are disclosed having utility as protease inhibitors in general and, more specifically, as serine protease inhibitors such as thrombin, elastase and Factor X inhibitors. In one embodiment, the .beta.-sheet mimetic is a thrombin inhibitor.

21 Claims, 5 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 4

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 10. Document ID: US 6610497 B1

L10: Entry 10 of 52 File: USPT Aug 26, 2003

US-PAT-NO: 6610497
DOCUMENT-IDENTIFIER: US 6610497 B1

TITLE: Angiotensin converting enzyme homolog and therapeutic and diagnostic uses therefor

DATE-ISSUED: August 26, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Acton; Susan L.	Lexington	MA		
Robison; Keith Earl	Wilmington	MA		
Hsieh; Frank Y.	Lexington	MA		

US-CL-CURRENT: 435/7.1; 436/501, 436/86, 530/313

ABSTRACT:

The present invention relates to the discovery of novel genes encoding an angiotensin converting enzyme, Angiotensin Converting Enzyme-2 (ACE-2). The invention provides therapeutics, prognostic and diagnostics methods for treating blood pressure related disorders as well as various types of allergic conditions, among others. Also disclosed are screening assays for identifying compounds for treating and preventing these conditions.

25 Claims, 21 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 17

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 11. Document ID: US 6599923 B2

L10: Entry 11 of 52 File: USPT Jul 29, 2003

US-PAT-NO: 6599923
DOCUMENT-IDENTIFIER: US 6599923 B2

TITLE: Pharmaceutical composition

DATE-ISSUED: July 29, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Ikeda; Hitoshi	Higashiosaka			JP
Sohda; Takashi	Takatsuki			JP
Odaka; Hiroyuki	Kobe			JP

US-CL-CURRENT: 514/342; 546/269.7

ABSTRACT:

Pharmaceutical composition which comprises an insulin sensitivity enhancer in combination with other antidiabetics differing from the enhancer in the mechanism of action, which shows a potent depressive effect on diabetic hyperglycemia and is useful for prophylaxis and treatment of diabetes.

6 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Claims | KWIC | Draw Ds

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☐ 12. Document ID: US 6592865 B2

L10: Entry 12 of 52 File: USPT Jul 15, 2003

US-PAT-NO: 6592865
DOCUMENT-IDENTIFIER: US 6592865 B2

TITLE: Methods and compositions for modulating ACE-2 activity

DATE-ISSUED: July 15, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Parry; Tom J.	Walkersville	MD		
Sekut; Les	Ijamsville	MD		

US-CL-CURRENT: 424/94.64; 514/15, 514/2

ABSTRACT:

The invention relates to the use of angiotensin II in combination with angiotesin 1-9 to potentiate angiotensin II activity. The invention also relates to the use of combinations of angiotensin II and angiotensin 1-9 to increase vasoconstriction and to treat disorders associated with low blood pressure.

5 Claims, 4 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 4

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 13. Document ID: US 6589938 B2

L10: Entry 13 of 52 File: USPT Jul 8, 2003

US-PAT-NO: 6589938
DOCUMENT-IDENTIFIER: US 6589938 B2

TITLE: Use of angiotensin I derivatives as an agent for the treatment and prevention of infarction-related cardiac injuries and disorders

DATE-ISSUED: July 8, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Sim; Meng Kwoon	Singapore			SG

US-CL-CURRENT: 514/15

ABSTRACT:

The present invention relates generally to a method for the treatment and/or prophylaxis of infarction-related cardiac injuries and disorders. More particularly, the present invention contemplates a method for the treatment and/or prophylaxis of myocardial infarction and heart failure and/or related conditions. The method of the present invention is practised by the administration of a derivative of angiotensin I. In a preferred embodiment, the angiotensin I is des-Aspartate-angiotensin I. The present invention further contemplates compositions for use in the treatment and/or prophylaxis of infarction-related cardiac injuries and disorders such as but not limited to myocardial infarction and heart failure.

13 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 14. Document ID: US 6586426 B1

L10: Entry 14 of 52 File: USPT Jul 1, 2003

US-PAT-NO: 6586426

DOCUMENT-IDENTIFIER: US 6586426 B1
** See image for Certificate of Correction **

TITLE: .beta.-sheet mimetics and use thereof as protease inhibitors

DATE-ISSUED: July 1, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kahn; Michael	Kirkland	WA		

US-CL-CURRENT: 514/230.5; 514/221, 514/222.2, 514/228.8, 514/359, 514/368, 514/369, 514/413, 514/464, 514/562, 562/560

ABSTRACT:

There are disclosed .beta.-sheet mimetics and methods relating to the same for imparting or stabilizing the .beta.-sheet structure of a peptide, protein or molecule. In one aspect, the .beta.-sheet mimetics are covalently attached at the end or within the length of the peptide or protein. The .beta.-sheet mimetics have utility as protease inhibitors generally, including activity as serine protease inhibitors such as thrombin, elastase and Factor X.

15 Claims, 3 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 3

☐ 15. Document ID: US 6495338 B1

L10: Entry 15 of 52 File: USPT Dec 17, 2002

US-PAT-NO: 6495338
DOCUMENT-IDENTIFIER: US 6495338 B1

TITLE: Drug screening and diagnosis based on paracrine tubular renin-angiotensin system

DATE-ISSUED: December 17, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Rohrwasser; Andreas	Salt Lake City	UT		
Morgan; Terry	Salt Lake City	UT		
Lalouel; Jean-Marc	Salt Lake City	UT		

US-CL-CURRENT: 435/23; 424/94.66, 436/86, 514/2, 530/316

ABSTRACT:

The present invention relates to a method for screening drugs for use in treating

hypertension using the tubular renin-angiotensinogen system identified by the present invention. The invention further relates to a method to diagnose sodium status and sensitivity in an individual by measuring urinary angiotensinogen or angiotensin-I.

2 Claims, 30 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 5

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 16. Document ID: US 6458923 B1

L10: Entry 16 of 52 File: USPT Oct 1, 2002

US-PAT-NO: 6458923
DOCUMENT-IDENTIFIER: US 6458923 B1
**** See image for Certificate of Correction ****

TITLE: Modified position (7) bradykinin antagonist peptides

DATE-ISSUED: October 1, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kyle; Donald James	Abington	MD		

US-CL-CURRENT: 530/314; 530/328, 530/335, 530/336, 530/337, 530/408, 530/807, 530/816

ABSTRACT:

The substitution of the L-Pro at the 7-position of the peptide hormone bradykinin or other substituted analogs of bradykinin with an isoquinoline derivative which converts bradykinin agonists into bradykinin antagonists. The invention further includes the novel 7-position modified bradykinin antagonists which increase enzyme resistance, antagonist potency, and/or specificity of the new bradykinin antagonists. The analogs produced are useful in treating conditions and diseases of a mammal and human in which an excess of bradykinin or related kinins are produced or injected as by insect bites.

4 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 17. Document ID: US 6288036 B1

L10: Entry 17 of 52 File: USPT Sep 11, 2001

US-PAT-NO: 6288036

DOCUMENT-IDENTIFIER: US 6288036 B1

TITLE: Bradykinin type peptides

DATE-ISSUED: September 11, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kyle; Donald James	Abingdon	MD		
Hiner; Roger Neal	Baltimore	MD		

US-CL-CURRENT: 514/15; 514/2, 514/803, 530/314, 530/328, 530/335, 530/336, 530/337, 530/408, 530/807, 530/816, 548/532

ABSTRACT:

The substitution of the L-Pro at the 7-position with D-Phe or D-Tic and substitution of the L-Phe at the 8-position with hydroxyproline ethers and thioethers of the peptide hormone bradykinin and other additional substituted analogs of bradykinin converts bradykinin agonists into bradykinin antagonists. The invention further includes additional modifications at other positions within the novel 7- and 8-position modified bradykinin antagonists, which increase enzyme resistance, antagonist potency, and/or specificity of the new bradykinin antagonists. The analogs produced are useful in treating conditions and diseases of a mammal and human in which an excess of bradykinin or related kinins are produced or injected as by insect bites.

17 Claims, 0 Drawing figures
Exemplary Claim Number: 1

☐ 18. Document ID: US 6245764 B1

L10: Entry 18 of 52 File: USPT Jun 12, 2001

US-PAT-NO: 6245764
DOCUMENT-IDENTIFIER: US 6245764 B1

TITLE: .beta.-sheet mimetics and use thereof as inhibitors of biologically active peptides or proteins

DATE-ISSUED: June 12, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kahn; Michael	Kirkland	WA		
Ogbu; Cyprian O.	Bellevue	WA		
Eguchi; Masakatsu	Bellevue	WA		
Kim; Hwa-Ok	Redmond	WA		
Boatman, Jr.; Patrick Douglas	Issaquah	WA		

US-CL-CURRENT: 514/248; 514/19, 514/221, 514/405

ABSTRACT:

There are disclosed .beta.-sheet mimetics and methods relating to the same for imparting or stabilizing the .beta.-sheet structure of a peptide, protein or molecule. In one aspect, .beta.-sheet mimetics are disclosed having utility as protease inhibitors in general and, more specifically, as serine protease inhibitors such as thrombin, elastase and Factor X inhibitors. In one embodiment, the .beta.-sheet mimetic is a thrombin inhibitor.

22 Claims, 5 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 4

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 19. Document ID: US 6194556 B1

L10: Entry 19 of 52 File: USPT Feb 27, 2001

US-PAT-NO: 6194556
DOCUMENT-IDENTIFIER: US 6194556 B1
**** See image for Certificate of Correction ****

TITLE: Angiotensin converting enzyme homolog and therapeutic and diagnostic uses therfor

DATE-ISSUED: February 27, 2001

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Acton; Susan Laurene	Lexington	MA		
Robison; Keith Earl	Wilmington	MA		

US-CL-CURRENT: 536/23.2; 435/252.3, 435/320.1, 536/23.4, 536/24.31, 536/24.33

ABSTRACT:

The present invention relates to the discovery of novel genes encoding an angiotensin converting enzyme, Angiotensin Converting Enzyme-2 (ACE-2). Therapeutics, diagnostics and screening assays based on these molecules are also disclosed.

40 Claims, 3 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 9

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 20. Document ID: US 6020331 A

L10: Entry 20 of 52 File: USPT Feb 1, 2000

US-PAT-NO: 6020331
DOCUMENT-IDENTIFIER: US 6020331 A

TITLE: .beta.-sheet mimetics and use thereof as protease inhibitors

DATE-ISSUED: February 1, 2000

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kahn; Michael	Kirkland	WA		

US-CL-CURRENT: 514/221; 514/248, 514/405, 544/235, 546/197, 548/312.4, 548/360.1, 562/562

ABSTRACT:

There are disclosed .beta.-sheet mimetics and methods relating to the same for imparting or stabilizing the .beta.-sheet structure of a peptide, protein or molecule. In one aspect, the .beta.-sheet mimetics are covalently attached at the end or within the length of the peptide or protein. The .beta.-sheet mimetics have utility as protease inhibitors generally, including activity as serine protease inhibitors such as thrombin, elastase and Factor X.

34 Claims, 3 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 21. Document ID: US 5817756 A

L10: Entry 21 of 52 File: USPT Oct 6, 1998

US-PAT-NO: 5817756
DOCUMENT-IDENTIFIER: US 5817756 A

TITLE: Pseudo- and non-peptide bradykinin receptor antagonists

DATE-ISSUED: October 6, 1998

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kyle; Donald James	Mountain View	CA		
Mavunkel; Babu Joseph	Sunnyvale	CA		
Chakravarty; Sarjavit	Sunnyvale	CA		
Lu; Zhijian	Scotch Plains	NJ		

US-CL-CURRENT: 530/331; 530/330

ABSTRACT:

The invention provides bradykinin antagonist compounds wherein many (or all) of the peptide bonds of bradykinin are eliminated to yield compounds which specifically compete with bradykinin for binding to the bradykinin receptor. More particularly, the invention relates to compounds having, in appropriate spatial arrangement, two positively charged moieties flanking a hydrophobic organic moiety and a moiety which mimics a beta turn conformation.

9 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 22. Document ID: US 5686565 A

L10: Entry 22 of 52 File: USPT Nov 11, 1997

US-PAT-NO: 5686565
DOCUMENT-IDENTIFIER: US 5686565 A

TITLE: Bradykinin antagonist pseudopeptide derivatives of aminoalkanoic acids and related olefins

DATE-ISSUED: November 11, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kyle; Donald James	Abingdon	MD		
Mavunkel; Babu Joseph	Timonium	MD		

US-CL-CURRENT: 530/328

ABSTRACT:

Pseudopeptide compounds based on a modified bradykinin sequence are potent bradykinin receptor antagonist. All or a portion of the amino acids at positions 2 through 5 of the bradykinin sequence are replaced by 2-pyrrolidinyl and/or amino-alkanoic acid or related olefinic derivatives to reduce the peptidic nature of the compounds.

The analogs produced are useful in treating conditions and diseases of a mammal and human in which an excess of bradykinin or related kinins are produced or injected such as by insect bites.

2 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 23. Document ID: US 5610142 A

L10: Entry 23 of 52 File: USPT Mar 11, 1997

US-PAT-NO: 5610142
DOCUMENT-IDENTIFIER: US 5610142 A

TITLE: Bradykinin antagonist pseudopeptide derivatives of substituted 4-keto-1,3,8-triazaspiro[4.5]decan-3-alkanoic acids

DATE-ISSUED: March 11, 1997

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Mavunkel; Babu J.	Baltimore	MD		
Lu; Zhijian	Scotch Plains	NJ		
Kyle; Donald J.	Abingdon	MD		

US-CL-CURRENT: 514/16; 514/15, 514/17, 530/314, 530/328

ABSTRACT:

Novel compounds with as few as three natural amino acids that incorporate a substituted 4-keto-1,3,8-triazaspiro[4.5]decan-3-alkanoyl bridge in place of selected fragments of peptidic bradykinin receptor antagonists are pseudopeptides with potent bradykinin receptor antagonist actions. These pseudopeptides and their pharmaceutical compositions are of benefit in treating conditions and diseases of mammals, including humans, in which an excess of bradykinin or a related kinin is produced endogenously or is received exogenously, for example via insect bite.

7 Claims, 0 Drawing figures
Exemplary Claim Number: 1,7

☐ 24. Document ID: US 5552383 A

L10: Entry 24 of 52 File: USPT Sep 3, 1996

US-PAT-NO: 5552383
DOCUMENT-IDENTIFIER: US 5552383 A

TITLE: Bradykinin antagonist pseudopeptide derivatives of aminoalkanoic acids and related olefins

DATE-ISSUED: September 3, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kyle; Donald J.	Abingdon	MD		
Mavunkel; Babu J.	Baltimore	MD		

US-CL-CURRENT: 514/15; 514/16, 530/314, 530/328

ABSTRACT:

Pseudopeptide compounds based on a modified bradykinin sequence are potent bradykinin receptor antagonists. All or a portion of the amino acids at postions 2 through 5 of the bradykinin sequence are replaced by 2-pyrrolidinyl and/or amino-alkanoic acid or related olefinic derivatives to reduce the peptidic nature of the compounds.

The analogs produced are useful in treating conditions and diseases of a mammal and human in which an excess of bradykinin or related kinins are produced or injected such as by insect bites.

9 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. De

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☐ 25. Document ID: US 5543496 A

L10: Entry 25 of 52 File: USPT Aug 6, 1996

US-PAT-NO: 5543496
DOCUMENT-IDENTIFIER: US 5543496 A

TITLE: Cyclic bradykinin antagonist peptides

DATE-ISSUED: August 6, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kyle; Donald J.	Abingdon	MD		
Chakravarty; Sarvajit	Baltimore	MD		

US-CL-CURRENT: 530/314; 530/317, 930/270

ABSTRACT:

Cyclic compounds based on a modified bradykinin sequence are potent bradykinin receptor antagonists. Amino acid substitutions are made at postions 2 and 5 or 6 to facilitate the cyclization of the peptide through covalent bonding of the amino acid side chains.

The analogs produced are useful in treating conditions and diseases of a mammal and human in which an excess of bradykinin or related kinins are produced or injected such as by insect bites.

1 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. De

☐ 26. Document ID: US 5541286 A

L10: Entry 26 of 52 File: USPT Jul 30, 1996

US-PAT-NO: 5541286
DOCUMENT-IDENTIFIER: US 5541286 A

TITLE: Bradykinin antagonist pseudopeptide derivatives of olefinic aminoalkanoic acids

DATE-ISSUED: July 30, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kyle; Donald J.	Abingdon	MD		

US-CL-CURRENT: 530/314; 530/329, 530/330

ABSTRACT:

Pseudopeptide compounds based on a modified bradykinin sequence are potent bradykinin receptor antagonists. Amino acids at at positions 2 through 5 are replaced by olefinic aminoalkenoyl groups to reduce the peptide nature of the compounds.

The analogs produced are useful in treating conditions and diseases of a mammal and human in which an excess of bradykinin or related kinins are produced or injected such as by insect bites.

2 Claims, 0 Drawing figures
Exemplary Claim Number: 1

☐ 27. Document ID: US 5532124 A

L10: Entry 27 of 52 File: USPT Jul 2, 1996

US-PAT-NO: 5532124
DOCUMENT-IDENTIFIER: US 5532124 A
**** See image for Certificate of Correction ****

TITLE: Genetically engineered bacteria to identify and produce medically important agents

DATE-ISSUED: July 2, 1996

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Block; Timothy M.	Doylestown	PA		

Grafstrom; Robert H. Lansdowne PA

US-CL-CURRENT: 435/5; 435/184, 435/23, 435/244, 435/252.3, 435/34, 435/6, 435/68.1, 435/69.1, 435/69.2, 435/974

ABSTRACT:

Microorganisms modified such that their growth in selective media is dependent upon the inhibition of a medically important target function are provided and utilized in methods for the screening of potential medically important compounds.

11 Claims, 6 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 6

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 28. Document ID: US 5444048 A

L10: Entry 28 of 52 File: USPT Aug 22, 1995

US-PAT-NO: 5444048
DOCUMENT-IDENTIFIER: US 5444048 A

TITLE: Bradykinin antagonist pseudopeptide derivatives of olefinic aminoalkanoic acids

DATE-ISSUED: August 22, 1995

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kyle; Donald J.	Abingdon	MD		

US-CL-CURRENT: 514/16; 514/17, 514/18, 530/314, 530/323, 530/329, 530/332

ABSTRACT:

Pseudopeptide compounds based on a modified bradykinin sequence are potent bradykinin receptor antagonists. Amino acids at postions 2 through 5 are replaced by olefinic aminoalkenoyl groups to reduce the peptidic nature of the compounds.

The analogs produced are useful in treating conditions and diseases of a mammal and human in which an excess of bradykinin or related kinins are produced or injected such as by insect bites.

9 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 29. Document ID: US 5385889 A

L10: Entry 29 of 52 File: USPT Jan 31, 1995

US-PAT-NO: 5385889
DOCUMENT-IDENTIFIER: US 5385889 A

TITLE: Bradykinin antagonist peptides

DATE-ISSUED: January 31, 1995

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Kyle; Donald J.	Abingdon	MD		
Hiner; Roger N.	Baltimore	MD		

US-CL-CURRENT: 514/15; 435/107, 514/2, 514/20, 514/803, 530/314, 530/328, 548/532, 930/30

ABSTRACT:

The substitution of the L-Pro at the 7-position of the peptide hormone bradykinin or other substituted analogs of bradykinin with a D-configuration hydroxyproline ether or thioether converts bradykinin agonists into bradykinin antagonists. The invention further includes the intermediate compounds and additional modifications at other positions within the novel 7-position modified bradykinin antagonists which increase enzyme resistance, antagonist potency, and/or specificity of the new bradykinin antagonists. The analogs produced are useful in treating conditions and diseases of a mammal and human in which an excess of bradykinin or related kinins are produced or injected such as by insect bites.

21 Claims, 1 Drawing figures
Exemplary Claim Number: 1
Number of Drawing Sheets: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 30. Document ID: US 5371096 A

L10: Entry 30 of 52 File: USPT Dec 6, 1994

US-PAT-NO: 5371096
DOCUMENT-IDENTIFIER: US 5371096 A

TITLE: (3-pyridyl)tetrafuran-2-yl substituted carboxylic acids

DATE-ISSUED: December 6, 1994

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Vlattas; Isodoros	Summit	NJ		

US-CL-CURRENT: 514/336; 546/284.4, 546/284.7

ABSTRACT:

Disclosed are compounds of formula ##STR1## wherein R is OR' and R' is aryl-lower alkyl, biaryl-lower alkyl, lower alkyl or cycloalkyl-lower alkyl; or R is arylsulfonylamido;

n is 1, 2 or 3;

m is 1, 2 or 3;

Y is vinylene, ethylene or methyleneoxy; a stereoisomer or optical isomer thereof; and their pharmaceutically acceptable esters or salts; which are useful as thromboxane synthetase inhibitors and thromboxane receptor antagonists.

12 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Terms	Documents
angiotensin adj3 converting enzyme adj3 related carboxypeptidse or angiotensin adj3 converting enzyme adj3 2	52

Hit List

First Hit | Clear | Generate Collection | Print | Fwd Refs | Bkwd Refs | Generate OACS

Search Results - Record(s) 31 through 52 of 52 returned.

☐ 31. Document ID: US 5153214 A

Using default format because multiple data bases are involved.

L10: Entry 31 of 52 File: USPT Oct 6, 1992

US-PAT-NO: 5153214
DOCUMENT-IDENTIFIER: US 5153214 A
** See image for Certificate of Correction **

TITLE: Certain (arylsulfonamido- and imidazolyl-)-substituted carboxylic acids and derivatives thereof and use for suppressing thromboxane activity

DATE-ISSUED: October 6, 1992

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bhagwat; Shripad S.	Scotch Plains	NJ		
Main; Alan J.	Basking Ridge	NJ		
Rodriguez; Herman R.	New York	NY		

US-CL-CURRENT: 514/381; 514/399, 548/252, 548/253, 548/340.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 32. Document ID: US 5025025 A

L10: Entry 32 of 52 File: USPT Jun 18, 1991

US-PAT-NO: 5025025
DOCUMENT-IDENTIFIER: US 5025025 A
** See image for Certificate of Correction **

TITLE: (Arylsulfonamido- and pyridyl-)-substituted carboxylic acids and derivatives thereof and use for suppressing thromboxane activity

DATE-ISSUED: June 18, 1991

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Bhagwat; Shripad S.	Scotch Plains	NJ		
Main; Alan J.	Basking Ridge	NJ		
Rodriguez; Herman R.	New York	NY		

US-CL-CURRENT: 514/340; 514/347, 514/357, 546/268.4, 546/293, 546/335

ABSTRACT:

Disclosed are the compounds of formula ##STR1## wherein A represents lower alkylene; B represents oxygen, sulfur, lower alkylene, lower alkylene interrupted by oxygen, sulfur, sulfinyl or sulfonyl, (oxy-, sulfinyl-, sulfonyl- or thio)-lower alkylene, lower alkenylene, phenylene or a direct bond; M represents lower alkylene, lower alkylene interrupted by oxygen, sulfur, sulfinyl or sulfonyl, (oxy-, sulfinyl, sulfonyl- or thio)-lower alkylene, lower alkenylene or a direct bond; or one of A, B and M represents lower alkylidenylene and the other two independently represent lower alkylene; R represents hydrogen unless A, B or M represents lower alkylidenylene in which case R represents the second bond to the adjacent aklylidenylene unsaturated carbon atom; Het represents 1-imidazolyl, 3-pyridyl, or 1-imidazolyl or 3-pyridyl substituted by lower alkyl; Ar represents carbocyclic or heterocyclic aryl; pharmaceutically acceptable ester and amide derivatives thereof; the N-oxides of said compounds wherein Het represents optionally substituted pyridyl; the said compounds of formula I wherein COOH is replaced by 5-tetrazolyl; and the pharmaceutically acceptable salts; which are useful as thromboxane synthetase inhibitors and thromboxane receptor antagonists.

60 Claims, 0 Drawing figures
Exemplary Claim Number: 1,47

☐ 33. Document ID: US 4855286 A

L10: Entry 33 of 52 File: USPT Aug 8, 1989

US-PAT-NO: 4855286
DOCUMENT-IDENTIFIER: US 4855286 A
**** See image for Certificate of Correction ****

TITLE: Renin-inhibiting di- and tripeptides, a process for their preparation, agents containing them, and their use

DATE-ISSUED: August 8, 1989

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Wagner; Adalbert	Hofheim am Taunus			DE
Kleemann; Heinz-Werner	Kelsterbach			DE
Ruppert; Dieter	Kelkheim			DE
Scholkens; Bernward	Kelkheim			DE

US-CL-CURRENT: 514/19; 530/860, 548/495, 549/493, 549/494, 549/76, 549/77, 560/159, 560/24, 564/152, 564/154, 564/159, 564/94, 564/95

ABSTRACT:

The invention relates to compounds of the formula ##STR1## in which R.sup.1 is absent or denotes hydrogen, alkyl or acyl, A denotes an acyl radical or an amino

acid residue, B denotes an amino acid residue, and R.sup.2, R.sup.3 and R.sup.4 are as defined in the specification, and to their salts, to a process for their preparation, to pharmaceutical products containing them, and to their use as medicaments, and intermediates for the preparation of these compounds.

8 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. De

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☐ 34. Document ID: US 4584299 A

L10: Entry 34 of 52 File: USPT Apr 22, 1986

US-PAT-NO: 4584299
DOCUMENT-IDENTIFIER: US 4584299 A

TITLE: Method of treating heart failure and medicaments therefor

DATE-ISSUED: April 22, 1986

INVENTOR-INFORMATION:

NAME	CITY	STATE	ZIP CODE	COUNTRY
Steffen; Robert P.	Saline	MI		
Evans; Dale B.	Saline	MI		
Kaplan; Harvey R.	Ann Arbor	MI		
Weisbach; Jerry A.	Ann Arbor	MI		

US-CL-CURRENT: 514/252.05

ABSTRACT:

Method for treating heart failure by increasing myocardial contractility and cardiac output with the administration of a pharmaceutical composition containing a combination of active ingredients including a pyridazinone or pyridin-one cardiotonic agent and a tetrahydroisoquinoline-3-carboxylic or octahydro-1H-indole-2-carboxylic acid ACE inhibitor.

7 Claims, 0 Drawing figures
Exemplary Claim Number: 1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw. De

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☐ 35. Document ID: WO 2005032487 A2

L10: Entry 35 of 52 File: EPAB Apr 14, 2005

PUB-NO: WO2005032487A2
DOCUMENT-IDENTIFIER: WO 2005032487 A2
TITLE: ANGIOTENSIN-CONVERTING ENZYME-2 AS A RECEPTOR FOR THE SARS CORONAVIRUS

PUBN-DATE: April 14, 2005

INVENTOR-INFORMATION:

NAME	COUNTRY
FARZAN, MICHAEL	US
LI, WENHUI	US
MOORE, MICHAEL J	US

INT-CL (IPC): A61 K 0/

ABSTRACT:

CHG DATE=20050426 STATUS=O>The present invention is based upon the identification of human angiotensinconverting enzyme-2 (ACE-2) as a functional receptor for the SARS coronavirus. Transfection of cells with ACE-2 confers upon them the ability to support viral replication. In addition, assays performed using ACE-2 together with the S protein of the SARS virus or a fragment derived from the S protein can be used to identify inhibitors that block the interaction between virus and host cell.

☐ 36. Document ID: WO 2005097109 A1

L10: Entry 36 of 52 File: DWPI Oct 20, 2005

DERWENT-ACC-NO: 2005-778894
DERWENT-WEEK: 200579

TITLE: Enhancing expression of angiotensin converting enzyme 2 in kidneys and vasculature e.g. renal vasculature and podocytes, comprises administering angiotensin II antagonist

INVENTOR: BATLLE, D; WYSOCKI, J ; YE, M

PRIORITY-DATA: 2004US-558718P (April 1, 2004)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 2005097109 A1	October 20, 2005	E	046	A61K031/41

INT-CL (IPC): A61 K 31/41; A61 K 31/415; A61 K 31/519

ABSTRACTED-PUB-NO: WO2005097109A
BASIC-ABSTRACT:

NOVELTY - Enhancing (M1) expression of angiotensin converting enzyme 2 (ACE2) in the kidneys and vasculature (e.g. renal vasculature) and podocytes, comprises administering an angiotensin II antagonist.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for enhancing (M2) the

expression ratio of ACE2 to ACE in the kidneys which comprises administering an angiotensin II blocking amount of an angiotensin II antagonist, to a mammal in need of renal protection.

ACTIVITY - Nephrotropic; Hypotensive.

MECHANISM OF ACTION - Angiotensin II antagonist.

Tests are described, but no results are given.

USE - (M1) is useful for enhancing expression of ACE2 in the kidneys, vasculature e.g. renal vasculature and podocytes (claimed) or ameliorating kidney damage from diseases such as diabetes and renal hypertension.

ADVANTAGE - (M1) is useful for enhancing expression of ACE2 in the kidney, vasculature e.g. renal vasculature and podocytes of a mammal.

☐ 37. Document ID: US 20050282154 A1, WO 2005032487 A2

L10: Entry 37 of 52 File: DWPI Dec 22, 2005

DERWENT-ACC-NO: 2005-296021
DERWENT-WEEK: 200603

TITLE: Novel soluble angiotensin-converting enzyme-2, useful as functional receptor for severe acute respiratory syndrome SARS coronavirus for blocking binding of SARS virus to host cell

INVENTOR: FARZAN, M R; LI, W ; MOORE, M J ; FARZAN, M

PRIORITY-DATA: 2004US-0957880 (October 5, 2004), 2003US-508281P (October 6, 2003)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 20050282154 A1	December 22, 2005		000	C12Q001/70
WO 2005032487 A2	April 14, 2005	E	037	A61K000/00

INT-CL (IPC): A61 K 0/00; C12 N 7/01; C12 N 15/86; C12 Q 1/70

ABSTRACTED-PUB-NO: WO2005032487A
BASIC-ABSTRACT:

NOVELTY - Soluble angiotensin-converting enzyme-2 (ACE-2) (I) consisting essentially of a fully defined 702 amino acids (SEQ ID No.2) sequence given in specification, where the soluble ACE-2 is detectably labeled, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) growing the severe acute respiratory syndrome (SARS) coronavirus in cell;

(2) assaying a test compound for its ability to block the binding of the SARS protein to the human ACE-2 receptor;

(3) blocking the binding of SARS virus to a host cell by contacting the host cell with an ACE-2 inhibitor;

(4) a substantially purified ACE-2 soluble protein (II), consisting essentially of (SEQ ID No.2);

(5) an antibody obtained by administering (II) to an animal capable of antibody production;

(6) a substantially purified polynucleotide consisting essentially of nucleotide encoding (II);

(7) a vector (III) comprising a promoter operably linked to a coding sequence, where the coding sequence encodes a protein having sequence of (SEQ ID No.2); and

(8) a host cell transformed with (III).

ACTIVITY - Virucide. No supporting data is given.

MECHANISM OF ACTION - ACE-2 inhibitor.

USE - (I) is useful for detecting the presence of SARS coronavirus in a test preparation or a liquid test preparation and for blocking the binding of SARS virus to a host cell (claimed).

☐ 38. Document ID: US 20050113298 A1, WO 2005028497 A2

L10: Entry 38 of 52 File: DWPI May 26, 2005

DERWENT-ACC-NO: 2005-254113
DERWENT-WEEK: 200535

TITLE: New angiotensin-converting enzyme 2 binding peptide comprising amino acid sequence identical to severe acute respiratory syndrome S (SARS S) protein, useful for inhibiting binding of S protein of SARS to host cell receptor

INVENTOR: FARZAN, M R; LI, W ; FARZAN, M

PRIORITY-DATA: 2003US-502610P (September 15, 2003), 2004US-0939113 (September 13, 2004)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 20050113298 A1	May 26, 2005		000	A61K038/17
WO 2005028497 A2	March 31, 2005	E	038	C07K000/00

INT-CL (IPC): A61 K 38/17; C07 H 21/04; C07 K 0/00; C07 K 14/705; C07 K 16/40

ABSTRACTED-PUB-NO: WO2005028497A
BASIC-ABSTRACT:

NOVELTY - A substantially pure angiotensin-converting enzyme 2 (ACE2) binding peptide (I) comprising an amino acid sequence identical to a severe acute respiratory syndrome S (SARS S) protein having a fully defined 1255 amino acid (SEQ ID No. 1) sequence given in the specification, is new.

DETAILED DESCRIPTION - A substantially pure angiotensin-converting enzyme 2 (ACE2) binding peptide (I) comprises an amino acid sequence identical to a severe acute respiratory syndrome S (SARS S) protein having a fully defined 1255 amino acid (SEQ ID No. 1) sequence given in the specification, where (a) the sequence begins at its N terminal at an amino acid in SEQ ID No. 1 chosen from amino acid 318-326, and extends toward the C terminal to at least amino acid 491 and no further than amino acid 672 in SEQ ID No. 1, or (b) the sequence ends at its C terminal at an amino acid in SEQ ID No. 1 chosen from amino acid 491-510, and extends toward the N terminal to at least amino acid 326 and no further than amino acid 12 in SEQ ID No. 1.

INDEPENDENT CLAIMS are also included for the following:

(1) a fusion polypeptide (II) consisting essentially of (I) fused to a marker amino acid sequence;

(2) a substantially pure polynucleotide (III) consisting essentially of nucleotides encoding (I) or (II);

(3) a vector (V1) comprising a promoter operably linked to (III);

(4) a host cell (HC) transformed with V1;

(5) assaying a test compound for its ability to inhibit the binding of the SARS S protein to its receptor to its receptor, involves (a) incubating a host cell expressing a receptor that binds to the S protein, with a solution comprising (II) and test compound, (b) removing the solution from the cells, after incubation step, (c) assaying the cells of step (c) to determine the amount of label present, and (d) comparing the results of step (c) to results obtained using cells prepared in the same manner but which are incubated in the absence of the test compound;

(6) a fluorescence-activated cells sorting (FACS) assay (M1) for determining the ability of a test compound to inhibit the binding of the SARS S protein to its receptor, involves (a) incubating cells that express a receptor that binds with specificity to the SARS S protein, in a solution comprising the test compound and (I) which is labeled in a manner that permits detection by fluorometry, (b) removing the solution from the cells, (c) assaying the cells of step (c) to determine the amount of label present, and (d) comparing the results of step (c) to results from cells prepared in the same manner but which are incubated in the absence of the test compound; and

(7) an antibody (IV) obtained by the process of injecting (I) to an animal capable of producing antibodies.

ACTIVITY - Respiratory-Gen.; Virucide.

MECHANISM OF ACTION - Inhibits binding of SARS S protein to host cell receptor (claimed); Angiotensin-converting enzyme 2 (ACE2)-inhibitor. In vitro analysis of angiotensin-converting enzyme 2 (ACE2) binding peptide in blocking S-protein mediated infection was carried out as follows. The 293T cells were transfected with a plasmid encoding severe acute respiratory syndrome (SARS)-CoV S protein, together with plasmid encoding the genome of simian immunodeficiency virus (SIV), modified by deletion of the env gene and by replacement of the nef gene with that for green fluorescent protein (GFP). Supernatants of transfected cells were harvested, and viral reverse-transcriptase activity was measured. Supernatants containing S-

protein-pseudotyped SIV were added to ACE2- or mock-transfected 293T cells in the presence or absence of the indicated concentrations of ACE2 binding peptide (12-237 or its 318-510 variants of SARS S1-Ig protein). Media was changed the following day and GFP expression in infected cells was measured two days later by flow cytometry. The results indicated that the peptide inhibited infection by S protein-pseudotyped lentivirus.

USE - (I) or (II) is useful for inhibiting the binding of the S protein of SARS to a host cell receptor, which involves contacting the receptor with (I) or (II). (I) is useful in FACS assay for identifying cells having a receptor that binds the S protein of SARS, which involves incubating cells with a solution comprising (I) which is labeled in a manner that permits detection by fluorometry, removing the solution from the cells, and assaying the cells of above step to determine the amount of label present. (I) is useful in FACS assay for determining the ability of a test compound to inhibit the binding of the SARS S protein to its receptor. (II) is useful for determining whether a cell has a receptor that binds to the SARS S protein, which involves incubating the cell with a solution comprising (II), removing the solution from the cells, and assaying the cell of above step, to determine the amount of peptide bound. (II) is useful for assaying a test compound for its ability to inhibit the binding of the SARS S protein to its receptor (claimed). (I) is useful in vaccines for preventing SARS in humans. (IV) is useful for purifying SARS S protein, and in immunoassay for detecting the presence of SARS protein, either in free state are attached to virus.

ADVANTAGE - (I) effectively binds to the cellular receptors (ACE receptor) of the SARS S protein, thus blocking the binding of SARS S protein to the host cell receptor. (I) prevents interaction between virus and the host cells, in vivo or in vitro.

☐ 39. Document ID: WO 2005020971 A1

L10: Entry 39 of 52 File: DWPI Mar 10, 2005

DERWENT-ACC-NO: 2005-214422
DERWENT-WEEK: 200522

TITLE: Use of angiotensin II type 1 receptor antagonist e.g. candesartan and an angiotensin converting enzyme inhibitor e.g. enalapril for preventing non-fatal myocardial infarction in a chronic heart failure patient

INVENTOR: GRANGER, C; HELD, P ; MCMURRAY, J ; MICHELSON, E ; OESTERGREN, J ; OLOFSSON, B ; PFEFFER, M ; SWEDBERG, K ; YUSEF, S

PRIORITY-DATA: 2003SE-0002331 (August 29, 2003)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 2005020971 A1	March 10, 2005	E	026	A61K031/00

INT-CL (IPC): A61 K 31/00; A61 K 31/401; A61 K 31/41; A61 K 31/4164; A61 K 31/4196; A61 K 31/437; A61 K 31/506; A61 K 31/519

ABSTRACTED-PUB-NO: WO2005020971A

BASIC-ABSTRACT:

NOVELTY - Prevention of myocardial infarction comprises administration of an angiotensin II type 1 receptor antagonist (1) and an angiotensin converting enzyme (2) inhibitor.

ACTIVITY - Cardiant; Cardiovascular-Gen.; Hypotensive.

MECHANISM OF ACTION - Angiotensin II type 1 receptor antagonist and an angiotensin converting enzyme inhibitor.

USE - (1 and 2) as medicaments are useful for preventing myocardial infarction (preferably non-fatal myocardial infarction) in a chronic heart failure patient (claimed). (1) interferes with rennin-angiotensin system and is useful to treat cardiovascular diseases particularly arterial hypertension. The ability of (1) to prevent the non-fatal myocardial infarction was tested in 49 patients along with a control group. The results showed that the risk of non-fatal myocardial infarction was 48.4% lower in 2-ethoxy-3-methyl-3H-benzoimidazole-4-carbo- xylic acid 1-cyclohexyloxycarbonyloxy-ethyl ester treated group than the control.

ADVANTAGE - (1) and (2) are useful in preventing non-fatal myocardial infarction when compared to the drugs that prevents or treats the myocardial infarction, which results in death.

☐ 40. Document ID: WO 2005018538 A2

L10: Entry 40 of 52 File: DWPI Mar 3, 2005

DERWENT-ACC-NO: 2005-214146
DERWENT-WEEK: 200522

TITLE: New polypeptide that binds to angiotensin-converting enzyme 2 (ACE2), useful in preparing a composition for diagnosing or treating Severe Acute Respiratory Syndrome (SARS)

INVENTOR: CHU, Y L; LAI, W ; LI, F Q

PRIORITY-DATA: 2003US-524614P (November 25, 2003), 2003US-475486P (June 4, 2003)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 2005018538 A2	March 3, 2005	E	039	A61K000/00

INT-CL (IPC): A61 K 0/00

ABSTRACTED-PUB-NO: WO2005018538A
BASIC-ABSTRACT:

NOVELTY - A new isolated polypeptide comprises any one of the 38 fully defined sequences having 7-31 amino acids (SEQ ID NOS: 1-32) or 14 (SEQ ID No: 39) or 17 (SEQ ID No: 109, 110, 111, 112 or 113) and binds to angiotensin-converting enzyme 2 (ACE2), where the polypeptide comprises up to 150 amino acid residues.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a bioconjugate comprising a hyaluronic acid polymer conjugated to the polypeptide;

(2) an article of manufacture comprising a solid support and the bioconjugate, which is immobilized on a surface of the solid support;

(3) a method of detecting the presence of anti-Severe Acute Respiratory Syndrome (SARS) antibodies in a sample;

(4) a pharmaceutical composition comprising the isolated polypeptide, bioconjugate or anti-SARS antibodies;

(5) a method of isolating anti-SARS antibodies;

(6) a method of immunizing a mammal against the SARS virus; and

(7) a method of treating SARS.

ACTIVITY - Respiratory-Gen.; Virucide.

No biological data given.

MECHANISM OF ACTION - None given.

USE - The polypeptide is useful in preparing a composition for diagnosing or treating Severe Acute Respiratory Syndrome (claimed).

☐ 41. Document ID: NO 200600922 A, EP 1367063 A1, WO 2005012333 A2

L10: Entry 41 of 52 File: DWPI Feb 24, 2006

DERWENT-ACC-NO: 2004-024726
DERWENT-WEEK: 200620

TITLE: Industrial synthesis of the angiotensin converting enzyme inhibitor perindopril, in 2-stage process from octahydro-1H-indole-2-carboxylic acid via new or known N-substituted propionyl derivative intermediate

INVENTOR: DUBUFFET, T; FUGIER, C ; LANGLOIS, P

PRIORITY-DATA: 2003EP-0291931 (July 31, 2003)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
NO 200600922 A	February 24, 2006		000	C07D209/00
EP 1367063 A1	December 3, 2003	F	009	C07K005/06
WO 2005012333 A2	February 10, 2005	F	000	C07K005/06

INT-CL (IPC): C07 D 209/00; C07 D 209/02; C07 D 209/42; C07 K 5/06

ABSTRACTED-PUB-NO: EP 1367063A
BASIC-ABSTRACT:

NOVELTY - Industrial synthesis of perindopril (I) involves: (a) reacting a (2S, 3aS, 7aS)-octahydro-1H-indole-2-carboxylic acid compound (II) with a 2(R)-substituted propionyl chloride (III) in presence of base; and (b) reacting the obtained (2S, 3aS, 7aS)-1-(2-substituted propionyl)-octahydro-1H-indole-2-carboxylic acid compound (IV) with ethyl (2S)-2-aminopentanoate (V) to give (I) (if necessary after deprotection). Some compounds (IV) are new.

DETAILED DESCRIPTION - Industrial synthesis of perindopril of formula (I) or its salts involves:

(a) reacting (2S, 3aS, 7aS)-octahydro-1H-indole-2-carboxylic acid (or its ester) of formula (II) with a 2(R)-substituted propionyl chloride of formula (III) in presence of base; and

(b) reacting the obtained (2S, 3aS, 7aS)-1-(2-substituted propionyl)-octahydro-1H-indole-2-carboxylic acid (or its ester) of formula (IV) with ethyl (2S)-2-aminopentanoate of formula (V) to give (I) (if necessary after deprotection).

R = H, benzyl or 1-6C alkyl;

G = Cl, Br, OH, p-toluenesulfonyloxy, methanesulfonyloxy or trifluoromethanesulfonyloxy.

An INDEPENDENT CLAIM is included for intermediates of formula (IV; G = Cl, p-toluenesulfonyloxy or methanesulfonyloxy).

ACTIVITY - Hypotensive; Cardiovascular-Gen.; Cardiant.

MECHANISM OF ACTION - Angiotensin converting enzyme inhibitor.

USE - (I) (described in EP49658) is an angiotensin converting enzyme inhibitor useful in treating cardiovascular diseases, especially arterial hypertension and cardiac insufficiency.

ADVANTAGE - (I) is obtained from readily accessible starting compounds.

☐ 42. Document ID: US 6610497 B1

L10: Entry 42 of 52 File: DWPI Aug 26, 2003

DERWENT-ACC-NO: 2003-895335
DERWENT-WEEK: 200529

TITLE: Identification of compound that modulates bioactivity of angiotensin converting enzymes-2 polypeptide, by detecting modulation of the bioactivity of polypeptide that is contacted with test compound as compared to control

INVENTOR: ACTON, S L; HSIEH, F Y ; ROBISON, K E

PRIORITY-DATA: 1999US-0407427 (September 29, 1999), 1997US-0989299 (December 11, 1997), 1998US-0163648 (September 30, 1998)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 6610497 B1	August 26, 2003		096	G01N033/53

INT-CL (IPC): G01 N 33/53

ABSTRACTED-PUB-NO: US 6610497B
BASIC-ABSTRACT:

NOVELTY - A compound that modulates bioactivity of an angiotensin converting enzymes-2 (ACE-2) polypeptide is identified by contacting an ACE-2 polypeptide with a test compound under conditions for modulation of the bioactivity of the polypeptide; and detecting modulation of the bioactivity of the polypeptide by the test compound as compared to a control.

DETAILED DESCRIPTION - An INDEPENDENT CLAIM is also included for modulating a bioactivity of an ACE-2 polypeptide by contacting the ACE-2 polypeptide with a compound that has been identified.

USE - The method is for identifying a compound that modulates the bioactivity of an angiotensin converting enzymes-2 peptides.

ADVANTAGE - The inventive method identifies other potential substrates of an ACE-2 polypeptides and product of the enzymatic reaction. The comparison of the mass spectra of the test compound with that of the reaction mixture after incubation indicates whether the test compound was converted into new compound, in which case the test compound is a substrate of the ACE-2 polypeptide.

☐ 43. Document ID: US 6900033 B2, WO 200298448 A1, US 20030138894 A1, US 2004121429 A9, AU 2002345443 A1

L10: Entry 43 of 52 File: DWPI May 31, 2005

DERWENT-ACC-NO: 2003-140552
DERWENT-WEEK: 200536

TITLE: Novel angiotensin converting enzyme-2 binding polypeptide useful for treating, preventing or ameliorating hypertension, congestive heart failure, stroke, left ventricular failure and atherosclerotic heart disease

INVENTOR: ALBERT, V R; HUANG, L ; PARRY, T J ; ROSEN, C A ; SANYAL, I ; SEKUT, L ; WESCOTT, C R

PRIORITY-DATA: 2001US-294976P (June 4, 2001), 2002US-0158825 (June 3, 2002)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 6900033 B2	May 31, 2005		000	A61K038/16
WO 200298448 A1	December 12, 2002	E	248	A61K038/12
US 20030138894 A1	July 24, 2003		000	A61K038/16
US 2004121429 A9	June 24, 2004		000	A61K038/16

AU 2002345443 A1 December 16, 2002 000 A61K038/12

INT-CL (IPC): A61 K 38/12; A61 K 38/16; C07 K 14/00; C12 N 5/06; C12 N 9/64; C12 P 21/02

ABSTRACTED-PUB-NO: WO 200298448A
BASIC-ABSTRACT:

NOVELTY - An isolated angiotensin converting enzyme (ACE)-2 binding polypeptide (I), is new.

DETAILED DESCRIPTION - (I) comprises or consists of an amino acid sequence Gly-Asp-Arg-Leu-His-Cys-Lys-Pro-Gln-Arg-Gln-Ser-Pro-Trp-Met-Lys-Cys-Gln-H- is-Leu-Asp-Pro-Glu-Gly-Gly-Gly, Gly-Asp-Leu-His-Ala-Cys-Arg-Pro-Val-Arg-Gl- y-Asp-Pro-Trp-Trp-Ala-Cys-Thr-Leu-Gly-Asp-Pro-Glu-Gly-Gly-Gly, Gly-Asp-Arg-Tyr-Leu-Cys-Leu-Pro-Gln-Arg-Asp-Lys-Pro-Trp-Lys-Phe-Cys-Asn-T- rp-Phe-Asp-Pro-Glu-Gly-Gly-Gly, Gly-Asp-Tyr-Ser-His-Cys-Ser-Pro-Leu-Arg-Ty- r-Tyr-Pro-Trp-Trp-Lys-Cys-Thr-Tyr-Pro-Asp-Pro-Glu-Gly-Gly-Gly, Gly-Asp-Gly-Phe-Thr-Cys-Ser-Pro-Ile-Arg-Met-Phe-Pro-Trp-Phe-Arg-Cys-Asp-Leu-Gly-Asp-Pro-Glu-Gly-Gly-Gly or Gly-Asp-Phe-Ser-Pro-Cys-Lys-Ala-Leu-Arg-- His-Ser-Pro-Trp-Trp-Val-Cys-Pro-Ser-Gly-Asp-Pro-Glu-Gly-Gly-Gly.

ACTIVITY - Hypotensive; Cardiant; Cerebroprotective; Antiatherosclerotic; Analgesic; Antiinflammatory; Nephrotropic; Hypertensive; Vasotropic; Cytostatic; Antiasthmatic; Antiallergic; Neuroprotective; Antiparkinsonian; Nootropic; Antirheumatic; Antiarthritic; Antigout; Tranquilizer; Vulnerary; Antidiabetic; Dermatological; Immunosuppressive; Hepatotropic; Anti-HIV; Antibacterial.

MECHANISM OF ACTION - Inhibitor of ACE-2 mediated enzymatic action; Inhibitor of aberrant expression of ACE-2.

No suitable data given.

USE - (I) is useful for treating, preventing or ameliorating hypertension, congestive heart failure, stroke, left ventricular failure and atherosclerotic heart disease in an animal (claimed). (I) is useful for detecting, isolating, or purifying ACE-2 proteins or ACE-2 like polypeptides in solutions, mixtures, or biological samples. (I) is also useful for inhibiting or reducing stenosis, pain, inflammatory reactions, abnormal histamine release, vasoconstriction, diseases or disorders related to vasoconstriction, and diseases and/or disorders associated with aberrant action of ACE-2. (I) is useful to detect, isolate, or remove ACE-2 target proteins in solutions, and also to identify epitopes of ACE-2. (I) is also useful to detect, diagnose, prognose, or monitor cardiovascular diseases, and disorders associated with aberrant aldosterone activity, or cell proliferation. (I) is useful for preventing and treating renal disorders, e.g., acute glomerulonephritis, and diseases associated with it. (I) is also useful to assay protein levels in a biological sample, for immunophenotyping of cell lines and biological samples by their ACE-2 expression, and for identifying cells, such as cardiac myocytes, endothelial and epithelial cells of Bowman's capsule. (I) is useful for treating, preventing, or ameliorating diseases or disorders associated with hypotensin, ischemia, asthma, allergy, multiple sclerosis, cancers, Parkinson's and Alzheimer's diseases, rheumatoid arthritis, gout, trauma, dermatitis, diabetes mellitus, Sjogren's syndrome, Addison's disease, chronic active hepatitis, Crohn's disease, sarcoidosis, AIDS, and sepsis.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 44. Document ID: AU 2002249793 A1, WO 200261131 A2, US 20030113726 A1

L10: Entry 44 of 52 File: DWPI Aug 12, 2002

DERWENT-ACC-NO: 2002-619265
DERWENT-WEEK: 200427

TITLE: New isolated nucleic acid with at least one polymorphic position, useful for detecting, diagnosing and treating disorders such as angioedema, cancer, viral, bacterial or fungal infection, cardiovascular and autoimmune diseases

INVENTOR: HUI, L; MA-EDMONDS, M ; PERRONE, M H ; POWELL, J R ; SWANSON, B N ; TSUCHIHASHI, Z ; ZERBA, K E ; PERRONE, M ; POWELL, J ; SWANSON, B ; ZERBA, K

PRIORITY-DATA: 2001US-273037P (March 2, 2001), 2000US-251015P (December 4, 2000), 2001US-263678P (January 23, 2001), 2001US-0005956 (December 3, 2001)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
AU 2002249793 A1	August 12, 2002		000	C12Q001/68
WO 200261131 A2	August 8, 2002	E	977	C12Q001/68
US 20030113726 A1	June 19, 2003		000	C12Q001/68

INT-CL (IPC): C07 H 21/04; C07 K 14/47; C07 K 14/705; C12 N 5/06; C12 N 9/48; C12 N 9/64; C12 P 21/02; C12 Q 1/68

ABSTRACTED-PUB-NO: WO 200261131A
BASIC-ABSTRACT:

NOVELTY - Isolated nucleic acid (I) from a human gene encoding aminopeptidase P (XPNEP2), bradykinin receptor B1 (BDKRB1), tachykinin receptor B1 (TACR1), C1 esterase inhibitor (C1NH), kallikrein 1 (KLK1), bradykinin receptor B2 (BDKRB2), angiotensin converting enzyme 2 (ACE2) or protease inhibitor 4 (PI4), comprising at least one polymorphic position, is new.

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for:

(1) a probe that hybridizes to a polymorphic position as provided in the detailed summary of single nucleotide polymorphisms comprising additional 5' and 3' flanking genomic sequence;

(2) analyzing (M1) at least one nucleic acid sample comprising obtaining the sample from one or more individuals and determining the nucleic acid sequence at one or more polymorphic positions in a gene encoding a protein selected from XPNEP2, BDKRB1, TACR1, C1NH, BDKRB2, KLK1, ACE2 and PI4;

(3) constructing (M2) haplotypes using (I) comprising grouping at least two nucleic acids;

(4) identifying (M3) an individual at risk of developing a disorder upon administration of an ACE inhibitor and/or vasopeptidase inhibitor comprising:

(a) obtaining nucleic acid sample from the individual;

(b) amplifying one or more sequences from the sample using appropriate polymerase chain reaction (PCR) primers for amplifying across at least one polymorphic position, or determining the nucleotide present in at least one polymorphic position;

(c) comparing at least one polymorphic position with a known data set; and

(d) determining whether the result correlates with an increased or decreased risk for developing a disorder;

(5) a library of nucleic acids, each of which comprises one or more polymorphic positions within a gene encoding a human protein selected from XPNEP2, BDKRB1, TACR1, C1NH, BDKRB2, KLK1, ACE2 and PI4, where the polymorphic positions are selected from polymorphic positions as provided in the detailed summary of single nucleotide polymorphisms comprising additional 5' and 3' flanking genomic sequence;

(6) a kit for identifying an individual at risk of developing a disorder upon administration of an ACE inhibitor and/or vasopeptide inhibitor comprising sequencing primers and reagents, where the primers hybridize to at least one polymorphic position in a human gene selected from XPNEP2, BDKRB1, TACR1, C1NH, BDKRB2, KLK1, ACE2 and PI4; and

(7) genotyping (M4) an individual comprising obtaining a nucleic acid sample, determining the nucleotide present in at least one polymorphic position, and comparing at least one position with a known data set.

ACTIVITY - Thrombolytic; Anticoagulant; Immunosuppressive; Cytostatic; Cardiant; Hypotensive; Antianginal; Antiarteriosclerotic; Antiallergic; Virucide, antibacterial; Fungicide; Vulnerary; Antiinflammatory.

No suitable data given.

MECHANISM OF ACTION - Gene therapy; ACE-Inhibitor; Aminopeptidase-Inhibito- r; Bradykinin-antagonist; Kallikrein-Inhibitor; Tachykinin-Antagonist; Protease-Inhibitor.

USE - (I), (M1, M2, M3 and M4) and compositions are useful for detecting, diagnosing, treating, preventing various disorders such as angioedema and diseases which involve angiogenesis like hemangiomas, tumors, sarcomas, Crohn's disease, trachomas, and cardiovascular diseases like angina pectoris, hypertension, heart failure, myocardial infarction, ventricular hypertrophy, vascular diseases, aneurysm, embolism, thrombosis, coronary artery disease, arteriosclerosis and/or atherosclerosis, and hypersensitivity reactions, sepsis, autoimmune diseases, inflammatory arthritis, cancer, wounds, viral, bacterial or fungal infection, Chronic obstructive pulmonary disease (COPD) and enterocolitis. The polynucleotides are also useful for chromosome identification. The antibodies may be utilized for immunophenotyping of cell lines and biological samples.

☐ 45. Document ID: AU 2002239454 A8, WO 200239997 A2, AU 200239454 A, US 20040082496 A1

L10: Entry 45 of 52 File: DWPI Oct 6, 2005

DERWENT-ACC-NO: 2002-547572
DERWENT-WEEK: 200612

TITLE: Treating body weight disorder and increasing muscle mass comprises

administering angiotensin converting enzyme-2 modulating compound

INVENTOR: ACTON, S L; BROWN, J A ; DALES, N A ; GOULD, A E ; GUAN, B ; KADAMBI, V J ; OCAIN, T D ; PATANE, M ; SOLOMON, M ; STRICKER-KRONGRAD, A

PRIORITY-DATA: 2001US-371741P (October 19, 2001), 2000US-0704216 (November 1, 2000), 2001US-0870382 (May 29, 2001), 1999US-132034P (April 30, 1999), 1999US-171052P (December 16, 1999), 2001US-0999781 (October 31, 2001)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
AU 2002239454 A8	October 6, 2005		000	A61P003/04
WO 200239997 A2	May 23, 2002	E	395	A61K031/00
AU 200239454 A	May 27, 2002		000	A61K031/00
US 20040082496 A1	April 29, 2004		000	A61K031/00

INT-CL (IPC): A61 K 31/00; A61 K 31/198; A61 K 31/341; A61 K 31/381; A61 K 31/415; A61 K 31/4152; A61 K 31/421; A61 K 31/426; A61 K 31/428; A61 K 39/395; A61 P 3/04; C07 C 237/40; C07 D 213/55; C07 D 213/68; C07 D 231/06; C07 D 231/08; C07 D 231/12; C07 D 261/08; C07 D 263/32; C07 D 277/22; C07 D 277/82; C07 D 333/54

ABSTRACTED-PUB-NO: WO 200239997A
BASIC-ABSTRACT:

NOVELTY - Treating a body weight disorder, increasing muscle mass and decreasing body fat comprises administration of angiotensin converting enzyme (ACE)-2 modulating compound (I).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) a transgenic mouse comprising a mutation in an endogenous ACE-2 gene in which the mutation is introduced into the mouse by homologous recombination in a mouse embryonic stem cell, the mutation inactivates the gene and results in the lack of expression of a biologically active ACE-2 protein, and results in the mouse having a lower percentage of body fat than its nontransgenic counterpart, and

(2) a progeny mouse of the transgenic mouse containing the mutation that inactivates the ACE-2 gene and results in the lack of expression of a biologically active ACE-2 protein, and lowering the percentage of body fat than its nontransgenic counterpart.

ACTIVITY - Anorectic; Immunomodulator; Antidiabetic; Antilipemic; Cardiant; Nootropic; Neuroprotective; Antiparkinsonian; Anticonvulsant; Tranquilizer; Vulnerary; Antiinflammatory; Antimigraine; Cerebroprotective; Antidepressant; Neuroleptic; Antibacterial; Immunosuppressive; Analgesic; Antirheumatic; Osteopathic; Antiarthritic; Gynecological; Analgesic; Antiallergic; Antiarteriosclerotic; Antiasthmatic.

The effect of 2-(1-carboxy-2-(3-(3,5-dichlorobenzyl)-3H-imidazol-4-yl)-ethylamino)4-methyl-pentanoic acid (Ia) on appetite was studied as described in 1982. Gen. Pharmacol. 13:173. Male ICR mice weighing 20 plus or minus 2 g (10-12 weeks of age) were orally administered distilled water (20 ml/kg) (control) or (Ia) (100 mg/kg) along with a food mass prepared from ground chow, evaporated milk and sugar at a ratio of 1 kg:0.75 l:0.15 g. Food consumption was measured after 1, 3 and 6 hours.

The cumulative food consumption for test/control mice after 1, 3 and 6 hours was

2.22 plus or minus 0.13/3.67 plus or minus 0.18, 4.06 plus or minus 0.27/4.92 plus or minus 0.06 and 5.38 plus or minus 0.41/5.91 plus or minus 0.12 respectively. The results showed that administration of (Ia) reduced food intake by 40% after one hour and 18% after 3 hours as compared to that in control mice.

MECHANISM OF ACTION - ACE-2 modulator; ACE-2 antagonist; ACE-2 agonist.

USE - Used for treating body weight disorders, particularly obesity of grade at least 1, diabetes, atherosclerosis and a state associated with lipid metabolism (all claimed). The method is used for treating rapid weight loss, rapid weight gain, anorexia, cachexia, bulimia, generalized partial lipodystrophy, familial partial lipodystrophy, hypercholesterolemia, hyperlipidemia, an aberrant metabolic rate, congestive heart failure, chronic hear failure, left ventricular hypertrophy, acute heart failure, neurodegenerative disorders (e.g. neuropathies, Alzheimer's disease, Parkinson's disease, Huntington's disease, amyotropic lateral sclerosis, motor neuron disease, traumatic nerve injury, multiple sclerosis, acute disseminated encephalomyelitis, acute necrotizing hemorrhagic leukoencephalitis, dysmyelination disease, mitochondrial disease, migrainous disorder, stroke, aging, dementia, peripheral nervous system diseases, mental disorders e.g. depression and schizophrenia), diseases associated with peptide hormones or cytokine processing, myocardial infarction, cardiomyopathy, systemic inflammation response syndrome, sepsis, polytrauma, inflammatory bowel disease, acute and chronic pain, bone destruction in rheumatoid arthritis and osteoarthritis and periodontal disease, dysmenorrhea, premature labor, brain edema following focal injury, diffuse axonal injury, stroke, reperfusion injury, cerebral vasospasm after subarachnoid hemorrhage, allergic disorders including asthma, adult respiratory distress syndrome, wound healing and scar formation.

ADVANTAGE - (I) Decreases the appetite, increases muscle mass and decreases body fat of subject having body mass index of greater than 23 (preferably 24.9)kg/m2. (I) Interacts with ACE-2 with a Ki value of upto 1 (especially upto 0.025) mu M.

☐ 46. Document ID: AU 2001284794 A8, WO 200212471 A2, AU 200184794 A

L10: Entry 46 of 52 File: DWPI Oct 6, 2005

DERWENT-ACC-NO: 2002-257481
DERWENT-WEEK: 200612

TITLE: Isolated human polypeptide, known as angiotensin converting enzyme-2, useful for treating or preventing the development of an abnormal blood pressure or related diseases, e.g. hypertension, heart failure or myocardial infarction

INVENTOR: ACTON, S; HSIEH, F Y ; ROBISON, K E

PRIORITY-DATA: 2000US-0635501 (August 9, 2000)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
AU 2001284794 A8	October 6, 2005		000	C12N009/48
WO 200212471 A2	February 14, 2002	E	218	C12N009/00
AU 200184794 A	February 18, 2002		000	C12N009/00

INT-CL (IPC): A61 K 38/48; A61 P 9/02; C12 N 9/00; C12 N 9/48; C12 N 15/12; G01 N 33/50

ABSTRACTED-PUB-NO: WO 200212471A
BASIC-ABSTRACT:

NOVELTY - A new isolated human polypeptide, known as angiotensin converting enzyme-2 (ACE-2), is new.

DETAILED DESCRIPTION - A new isolated human polypeptide, known as angiotensin converting enzyme-2 (ACE-2), is new.

The polypeptide comprises an amino acid sequence:

(a) having an identity of at least 70% to the 805 amino acid sequence (I) fully defined in the specification;

(b) that is at least 90% identical to at least about 15 consecutive amino acid residues of (I); or

(c) that is at least 70% similar to at least about 50 consecutive amino acid residues of (I) and which has a bioactivity of an angiotensin converting enzyme 2 (ACE-2) polypeptide.

INDEPENDENT CLAIMS are also included for the following:

(1) an isolated nucleic acid comprising a nucleotide sequence, which is at least 70% identical to the entire nucleotide sequence having 3396 bp (II) or 2415 bp fully defined in the specification or its complement;

(2) methods for producing the polypeptide;

(3) a method for identifying an ACE-2 therapeutic comprising contacting an ACE-2 polypeptide with a test compound and determining an ACE-2 bioactivity, such that a difference in the bioactivity of the ACE-2 polypeptide contacted with the test compound relative to an ACE-2 polypeptide that was not contacted with the test compound, indicates that the test compound is an ACE-2 therapeutic;

(4) a method for modulating a bioactivity of an ACE-2 polypeptide comprising contacting an ACE-2 polypeptide with a compound, which has been identified in (4);

(5) a method for treating or preventing the development of an abnormal blood pressure or disease or disorder associated with it in a subject by administering to the subject a pharmaceutical composition comprising the ACE-2 therapeutic, such that the disease or disorder in the subject is treated or prevented;

(6) a method for determining whether a subject has or is at risk of developing a disease or condition, which is caused or contributed to by an aberrant ACE-2 activity comprising measuring in the subject or in a sample obtained from the subject at least one ACE-2 activity, where a difference in the ACE-2 activity relative to the ACE-2 activity in a normal subject indicates that the subject is at risk of developing a disease caused by or contributed to by an aberrant ACE-2 activity; and

(7) a method for identifying a substrate of an ACE-2 polypeptide comprising:

(a) contacting an ACE-2 polypeptide with a test compound in a reaction mixture under conditions in which the ACE-2 polypeptide is able to cleave a substrate; and

(b) determining the mass spectrum of the reaction mixture of step (a) or a part of

it, such that the presence of a lower peak characteristic of the test compound in the reaction mixture of step (a) relative to that in a reaction mixture that does not contain the ACE-2 polypeptide, indicates that the test compound is a substrate of the ACE-2 polypeptide.

ACTIVITY - Hypotensive; hypertensive; cardiant; antiarrhythmic; anti-inflammatory; analgesic.

No biological data given.

MECHANISM OF ACTION - Angiotensin converting enzyme modulator.

No biological data given.

USE - The polypeptide is useful in methods for treating or preventing the development of an abnormal blood pressure, or disease or disorder associated with it in a subject. The disease includes hypertension, hypotension, congestive heart failure, chronic heart failure, acute heart failure, myocardial infarction, atherosclerosis, arrhythmia or renal failure (all claimed). The polypeptide is also useful for treating inflammatory conditions or diseases relating to fertility.

☐ 47. Document ID: US 6194556 B1

L10: Entry 47 of 52 File: DWPI Feb 27, 2001

DERWENT-ACC-NO: 2001-210604
DERWENT-WEEK: 200529

TITLE: Novel genes encoding angiotensin converting enzyme-2 useful as antisense or antigene agents for therapeutics, diagnostics and screening assays

INVENTOR: ACTON, S L; ROBISON, K E

PRIORITY-DATA: 1997US-0989299 (December 11, 1997)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 6194556 B1	February 27, 2001		075	C12N015/11

INT-CL (IPC): C12 N 15/11; C12 N 15/57; C12 N 15/74; C12 N 15/79

ABSTRACTED-PUB-NO: US 6194556B
BASIC-ABSTRACT:

NOVELTY - An isolated nucleic acid molecule (I) comprising a 3396 or 2415 nucleotide sequence (S1), fully defined in the specification, and encoding angiotensin converting enzyme-2 (ACE-2) comprising an 805 residue amino acid sequence (S2), fully defined in the specification, is new.

DETAILED DESCRIPTION - An isolated nucleic acid molecule (I) comprising a 3396 or 2415 nucleotide sequence (S1), fully defined in the specification, and encoding angiotensin converting enzyme-2 (ACE-2) comprising an 805 residue amino acid sequence (S2), fully defined in the specification, is new. (I) comprises:

(a) S1;

(b) residues 136-2496 or 136-2301 of S1;

(c) at least 20 consecutive nucleotides of S1 with the proviso that the sequence is not selected from expression sequence tag (EST) sequences having GenBank accession number AA397955, AA420696, AA162058, AA416585, AA421125 or AA072298;

(d) a sequence contained in the insert of plasmid deposited under ATCC 209510;

(e) at least 20 nucleotides that hybridizes to S1 or its complement having ATCC designation number 209510, in 6 multiply SSC (sodium saline chloride) at 45 deg. C followed by a wash in 0.2 multiply SSC at 65 deg. C;

(f) a sequence encoding S2 or its naturally occurring allelic variant having ACE-2 activity; or

(g) the complement of (a), (b), (c), (d), (e), or (f).

INDEPENDENT CLAIMS are also included for the following:

(1) an isolated nucleic acid molecule (II) comprising S1 or a 2415 nucleotide sequence, fully defined in the specification, and a nucleotide sequence encoding heterologous polypeptide;

(2) a vector (III) comprising (II);

(3) a recombinant host cell (IV) comprising (II) operatively linked to a recombinant transcriptional regulating sequence; and

(4) a kit comprising (II) and instructions for use.

ACTIVITY - None given.

MECHANISM OF ACTION - Antisense gene therapy.

No biological data is given.

USE - (I) is useful as antisense or antigene agents for sequence specific modulation of gene expression or in the analysis of single base-pair mutations in the gene. (I) is useful in therapeutics, diagnostics and in screening assays.

☐ 48. Document ID: WO 200066104 A2, AU 200045002 A, NO 200105274 A, EP 1183019 A2, BR 200010166 A, KR 2002008168 A, JP 2002543120 W, CN 1377259 A, ZA 200109378 A, MX 2001010993 A1, US 6632830 B1, US 20040082496 A1

L10: Entry 48 of 52 File: DWPI Nov 9, 2000

DERWENT-ACC-NO: 2001-015901
DERWENT-WEEK: 200429

TITLE: New angiotensin converting enzyme-2 (ACE-2) modulating compounds, useful alone or in combination with ACE inhibitors for treating e.g. blood pressure

related disorders, chronic heart failure, inflammation and kidney disorders

INVENTOR: ACTON, S L; BROWN, J A ; DALES, N A ; GOULD, A E ; GUAN, B ; OCAIN, T D ; KADAMBI, V J ; PATANE, M ; SOLOMON, M ; STRICKER-KRONGRAD, A

PRIORITY-DATA: 1999US-171052P (December 16, 1999), 1999US-132034P (April 30, 1999), 2000US-0561759 (April 28, 2000), 2000US-0704216 (November 1, 2000), 2001US-0870382 (May 29, 2001), 2001US-371741P (October 19, 2001), 2001US-0999781 (October 31, 2001)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
WO 200066104 A2	November 9, 2000	E	118	A61K031/00
AU 200045002 A	November 17, 2000		000	
NO 200105274 A	December 28, 2001		000	C07C000/00
EP 1183019 A2	March 6, 2002	E	000	A61K031/00
BR 200010166 A	June 4, 2002		000	A61K031/00
KR 2002008168 A	January 29, 2002		000	A61K031/315
JP 2002543120 W	December 17, 2002		155	C07D233/64
CN 1377259 A	October 30, 2002		000	A61K031/00
ZA 200109378 A	January 29, 2003		146	A61K000/00
MX 2001010993 A1	July 1, 2003		000	A61K031/00
US 6632830 B1	October 14, 2003		000	A61K031/194
US 20040082496 A1	April 29, 2004		000	A61K031/00

INT-CL (IPC): A61 K 0/00; A61 K 31/00; A61 K 31/194; A61 K 31/198; A61 K 31/315; A61 K 31/341; A61 K 31/381; A61 K 31/405; A61 K 31/415; A61 K 31/4164; A61 K 31/4172; A61 K 31/4174; A61 K 31/4178; A61 K 31/426; A61 K 31/4402; A61 K 31/4406; A61 K 39/395; A61 P 1/00; A61 P 1/02; A61 P 5/30; A61 P 9/00; A61 P 9/02; A61 P 9/04; A61 P 9/08; A61 P 9/10; A61 P 9/12; A61 P 11/06; A61 P 13/12; A61 P 17/00; A61 P 19/02; A61 P 21/00; A61 P 25/04; A61 P 29/00; A61 P 37/08; A61 P 43/00; C07 C 0/00; C07 C 229/16; C07 C 229/26; C07 D 209/20; C07 D 213/55; C07 D 231/12; C07 D 233/64; C07 D 277/30; C07 D 307/54; C07 D 333/24; C07 D 413/04

ABSTRACTED-PUB-NO: WO 200066104A
BASIC-ABSTRACT:

NOVELTY - Angiotensin converting enzyme-2 (ACE-2)-modulating compounds (I) are new.

DETAILED DESCRIPTION - Angiotensin converting enzyme-2 (ACE-2)-modulating compounds of formula (I) are new.

Z = zinc coordinating moiety; and

L = amino acid mimicking moiety.

INDEPENDENT CLAIMS are also included for the following:

(1) ACE-2 inhibiting compounds of formula (II) or (III);

Z' = as for Z;

E = enzyme coordinating moiety;

A = auxiliary pocket binding moiety;

B = side chain binding pocket moiety;

R6 = OH or a protecting prodrug moiety;

R7 = H, COOH, arylaminocarbonyl, aroyl, aryl, alkylaminocarbonyl, aminocarbonyl, alkenylaminocarbonyl, OH, alkoxy, ether, SH, NH2 or heterocycle;

R8 = H or alkyl, and optionally linked to D' to form a cyclic structure;

R9 = lower alkyl or H;

Q = a bond, O, S, CHOH, CHSH, CHNH2, CHNHR3, CHNR3R4, NH, NR3, (CH2)n, O(CH2)n or (CH2)nO(CH2)n;

R3, R4 = optionally substituted 1-5C alkyl, 2-5C alkenyl, acyl, aryl, 3-8C ring, optionally substituted by up to 4 heteroatoms;

G = linking moiety;

M = anchor moiety;

J = a bond, alkyl, alkenyl or alkynyl;

D' = H, alkyl, alkenyl, alkynyl, aryl or heteroaryl, optionally linked to G, M or Q to form a ring;

t , q = 0-3;

n = 0-3;

p = 0-5;

(2) treating an ACE-2 associated state in a patient comprising administering one or more ACE-inhibiting compounds;

(3) inhibiting the hydrolysis of an ACE-2 target peptide comprising contacting ACE-2 with an ACE-2 inhibiting compound;

(4) treating an ACE-2 associated state in a patient comprising administering an ACE-2 inhibiting compound and an ACE inhibitor.

ACTIVITY - Cardiant; hypotensive; cytostatic; nephrotropic; dermatological; antiinflammatory; antirheumatic; antiarthritic; vulnerary; antiallergic; analgesic; osteopathic; gynecological; tocolytic; neuroprotective; immunosuppressive; antibacterial; antiinfertility.

MECHANISM OF ACTION - ACE-2 inhibitor.

2-(1-Carboxy-2-(methyl phenylamino)-ethylamino)-4-methylpentanoic acid (IIIa) exhibited Ki values of less than 1 micro M ((very good inhibition) for human ACE-2 activity, 1-10 micro M (good inhibition) for rat ACE-2, less than 50 micro M (some inhibition) for ACE activity, and of 10-50 micro M (good inhibition) for carboxypeptidase A activity. (ACE-2 is a carboxypeptidase).

USE - (I) may be administered either alone or in combination with a known ACE inhibitor to treat ACE-2 associated disorders. In (2), the ACE-2 associated state is associated with a blood pressure related disease or disorder; chronic heart

failure, left ventricular hypertrophy, acute heart failure or cardiomyopathy; a congestive heart failure; arterial hypertension; myocardial infarction; cell proliferation disorder, especially a smooth cell proliferation disorder, particularly vascular stenosis; kidney disease or disorder; kinetensin associated disorder (especially those caused by abnormal vascular permeability, local and systemic allergic reactions, eczema, asthma or anaphylactic shock), inflammation, especially inflammation associated with systemic inflammatory response syndromes (SIRS) polytrauma, inflammatory bowel disease, acute and chronic pain, bone destruction in rheumatoid and osteoarthritis, periodontal disease, dysmenorrhea, premature labor, brain edema following focal injury, diffuse azonal injury, allergic disorders, wound healing and scar formation (all claimed). Also stroke, reperfusion injury , cerebral vasospasm after subarachnoid hemorrhage, adult respiratory distress syndrome, infertility (or other disorders relating to gamete maturation) and cognitive disorders. The method in (4) is used to treat cell proliferation disorder, kidney disorder, kinetensin associated disorder, inflammation associated disorder, allergic disorder, blood pressure related disease or disorder or congestive heart failure (claimed).

ADVANTAGE - Several ACE inhibitors are currently available on the market (e.g. captopril, enalapril, fosinopril, linsinopril and ramipril) for treating blood pressure disorders. However, ACE inhibitors in large doses can cause a variety of undesirable secondary effects including nephrotic syndrome, membraneous glomerulonephritis, neprhritis, leukopenia and angioedema. By combining (I) with a known ACE inhibitor, the effective dose of the ACE inhibitor will be reduced thus decreasing the risk of potentially harmful side effects. In addition to such combination therapies, use of ACE-2 inhibitors alone is more efficacious and provide improved therapy for treating blood pressure disorders compared to currently available ACE inhibitors.

☐ 49. Document ID: US 6989363 B1, WO 200018899 A2, AU 200013113 A, JP 2002525108 W, MX 2001003113 A1, EP 1248837 A2, US 6884771 B1, US 20050147600 A1

L10: Entry 49 of 52 File: DWPI Jan 24, 2006

DERWENT-ACC-NO: 2000-293140
DERWENT-WEEK: 200607

TITLE: Isolated nucleic acid encoding angiotensin converting enzyme-2 (ACE-2) polypeptide useful for detecting an ACE-2 therapeutic for treating hypertension, congestive heart failure, myocardial infarction, atherosclerosis and renal failure

INVENTOR: ACTON, L S; HSIEH, F Y ; ROBISON, K E ; ACTON, S ; ACTON, S L

PRIORITY-DATA: 1998US-0163648 (September 30, 1998)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
US 6989363 B1	January 24, 2006		000	C07K014/00
WO 200018899 A2	April 6, 2000	E	138	C12N009/48
AU 200013113 A	April 17, 2000		000	C12N009/48
JP 2002525108 W	August 13, 2002		189	C12N015/09
MX 2001003113 A1	October 1, 2001		000	A61K038/16

EP 1248837 A2	October 16, 2002	E	000	C12N009/48
US 6884771 B1	April 26, 2005		000	A61K038/00
US 20050147600 A1	July 7, 2005		000	C12Q001/68

INT-CL (IPC): A61 K 38/00; A61 K 38/16; A61 K 38/17; A61 K 38/48; A61 K 45/00; A61 P 9/00; A61 P 9/02; A61 P 9/04; A61 P 9/10; A61 P 9/12; A61 P 13/12; A61 P 43/00; C07 H 21/04; C07 K 14/00; C07 K 14/435; C12 N 9/48; C12 N 9/50; C12 N 9/64; C12 N 15/09; C12 N 15/55; C12 P 21/00; C12 Q 1/37; C12 Q 1/68; G01 N 33/15; G01 N 33/50; G01 N 33/53; G01 N 33/537; G01 N 33/543; C12 N 9/50; C12 R 1:91

ABSTRACTED-PUB-NO: WO 200018899A
BASIC-ABSTRACT:

NOVELTY - An isolated nucleic acid (N1) comprising a nucleotide sequence at least 70% identical to the entire defined nucleotide sequences (I) or (II) of 3396 and 2415 base pairs respectively given in the specification or their complements, encodes an angiotensin converting enzyme-2 (ACE-2).

DETAILED DESCRIPTION - INDEPENDENT CLAIMS are also included for the following:

(1) an isolated polypeptide (P1) comprising an amino acid (aa) sequence with at least 70% identity with the defined protein sequence (III) of 805 aa given in the specification;

(2) an isolated polypeptide (P2) comprising an aa sequence with at least 90% identity with (III);

(3) an isolated polypeptide (P3) which comprises an aa sequence at least 70% similar to at least 50 consecutive residues of (III) and has a bioactivity of an ACE-2 polypeptide;

(4) a method for producing P1 or P2 comprising incubating a host cell which includes a nucleic acid encoding P2 operably linked to a regulatory element;

(5) a method for identifying an ACE-2 therapeutic comprising contacting an ACE-2 polypeptide with a test compound and determining an ACE-2 bioactivity so a difference in bioactivity of the ACE-2 polypeptide contacted with the test compound compared to free ACE-2 polypeptide indicates the test compound is an ACE-2 therapeutic;

(6) a method for modulating a bioactivity of an ACE-2 polypeptide comprising contacting an ACE-2 polypeptide with a compound identified by the method of (5);

(7) a method for treating or preventing the development of an abnormal blood pressure or disease or disorder associated with abnormal blood pressure comprising administering to the subject a pharmaceutical composition comprising an ACE-2 polypeptide;

(8) a method of determining whether a subject has or is at risk of developing a disease or condition caused or contributed to by an aberrant ACE-2 activity comprising measuring in the subject or in a sample obtained from the subject at least one ACE-2 activity, where a difference in the ACE-2 activity relative to that in a normal subject indicates the subject is at risk of developing such a disease; and

(9) a method of identifying a substrate of an ACE-2 polypeptide comprising:

(a) contacting an ACE-2 polypeptide with a test compound in a reaction mixture

under conditions in which the ACE-2 polypeptide is able to cleave a substrate; and

(b) determining the mass spectrum of the reaction mixture so that the presence of a lower peak characteristic of the test compound in the mixture relative to that of a reaction mixture that does not contain the ACE-2 polypeptide, indicates the test compound is a substrate of the ACE-2 polypeptide.

ACTIVITY - Hypotensive; cardiant; antiarteriosclerotic; nephrotropic.

No biological data is given.

MECHANISM OF ACTION - ACE-2 antagonist.

USE - The method for detecting an ACE-2 therapeutic is used to identify an ACE-2 antagonist (claimed). The ACE-2 therapeutic is used to treat hypertension, congestive heart failure, chronic heart failure, acute heart failure, myocardial infarction, atherosclerosis and renal failure (claimed).

☐ 50. Document ID: CZ 296274 B6, WO 9907365 A1, ZA 9807018 A, AU 9887688 A, NO 200000577 A, EP 1027047 A1, BR 9811926 A, CZ 200000406 A3, CN 1276724 A, KR 2001022582 A, JP 2001513498 W, AU 739295 B, NZ 502644 A, MX 2000001385 A1, US 20020137943 A1, HU 200201624 A2, US 6630498 B2, MX 212857 B, IL 134378 A, TW 570921 A, NO 317771 B1

L10: Entry 50 of 52 File: DWPI Feb 15, 2006

DERWENT-ACC-NO: 1999-167199
DERWENT-WEEK: 200615

TITLE: New eprosartan arginyl charge neutralisation complex - prepared by mixing eprosartan with L-arginine in water, useful for treating hypertension, congestive heart failure and renal failure

INVENTOR: GUDIPATI, M R; JUSHCHYSHYN, J M ; PALEPU, N R ; VENKATESH, G M ; JUSHCYSHYN, J M

PRIORITY-DATA: 1997US-054990P (August 6, 1997), 2000US-0485203 (February 3, 2000), 2001US-0017873 (December 12, 2001)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
CZ 296274 B6	February 15, 2006		000	C07D233/00
WO 9907365 A1	February 18, 1999	E	039	A61K031/415
ZA 9807018 A	April 28, 1999		036	C07D000/00
AU 9887688 A	March 1, 1999		000	A61K031/415
NO 200000577 A	February 29, 2000		000	C07D409/06
EP 1027047 A1	August 16, 2000	E	000	A61K031/415
BR 9811926 A	August 22, 2000		000	A61K031/415
CZ 200000406 A3	September 13, 2000		000	A61K031/4178
CN 1276724 A	December 13, 2000		000	A61K031/415

KR 2001022582 A	March 26, 2001	000	A61K031/415
JP 2001513498 W	September 4, 2001	043	C07D409/06
AU 739295 B	October 11, 2001	000	A61K031/415
NZ 502644 A	March 1, 2002	000	A61K031/4178
MX 2000001385 A1	June 1, 2001	000	A61K031/415
US 20020137943 A1	September 26, 2002	000	C07D409/02
HU 200201624 A2	December 28, 2002	000	A61K031/415
US 6630498 B2	October 7, 2003	000	A61K031/415
MX 212857 B	February 7, 2003	000	A61K031/415
IL 134378 A	February 19, 2004	000	C07D409/06
TW 570921 A	January 11, 2004	000	C07D409/06
NO 317771 B1	December 13, 2004	000	C07D409/06

HU 200201624 A2 , US 6630498 B2 INT-CL (IPC): A61 K 9/16; A61 K 9/20; A61 K 31/381; A61 K 31/415; A61 K 31/4164; A61 K 31/4178; A61 K 45/00; A61 P 9/00; A61 P 9/04; A61 P 9/10; A61 P 9/12; A61 P 13/00; A61 P 13/12; C07 D 0/00; C07 D 233/00; C07 D 233/02; C07 D 233/04; C07 D 233/64; C07 D 409/02; C07 D 409/06; C07 D 233:64; C07 D 333:24; C07 D 409/06

ABSTRACTED-PUB-NO: US20020137943A
BASIC-ABSTRACT:

NOVELTY - (E)- alpha -(2-n-butyl-1-((4-carboxyphenyl)methyl)-1H-imidazol-5 yl) methylene-2-thiophenepropionic acid (eprosartan) arginyl charge-neutralization-complex (I) is new. DETAILED DESCRIPTION - (E)- alpha -(2-n-butyl-1-((4 carboxyphenyl)methyl)-1H-imidazol-5-yl)methylene- 2 thiophenepropionic acid arginyl charge-neutralization-complex (I) is new: INDEPENDENT CLAIMS are also included for the following:compositions comprising (I) and a diuretic, calcium channel blocker, beta -adrenoceptor blocker, renin inhibitor or angiotensin converting enzyme inhibitor; and (2) compositions comprising eprosartan or its methanesulphonate salt, a charge neutralization-complexing agent and a carrier.

USE - (I) is an angiotensin II blocker and is useful for treating hypertension, congestive heart failure and renal failure (claimed), also left ventricular hypertrophy regression, diabetic nephropathy, diabetic retinopathy, macular degeneration, haemorrhagic stroke, and for primary and secondary prevention of infarction, prevention of atheroma progression and the regression of atheroma, prevention of restenosis after angioplasty or bypass surgery, improving cognitive function, angina, glaucoma and CNS disorders (e.g. anxiety).

ADVANTAGE - (I) has increased lipophilicity, better dissolution profile and increased in vitro permeability through rabbit colon, compared with eprosartan monomethanesulphonate salt (EM). In an in-vitro dissolution study using granules of (I) and granules of EM, results for % eprosartan dissolved after 45, 120 and 225 minutes respectively were 32.81, 36.24 and 100.63% for (I), compared with 17.77, 19.64 and 58.52% for EM.
ABSTRACTED-PUB-NO:

WO 9907365A EQUIVALENT-ABSTRACTS:

NOVELTY - (E)- alpha -(2-n-butyl-1-((4-carboxyphenyl)methyl)-1H-imidazol-5 yl) methylene-2-thiophenepropionic acid (eprosartan) arginyl charge-neutralization-complex (I) is new. DETAILED DESCRIPTION - (E)- alpha -(2-n-butyl-1-((4 carboxyphenyl)methyl)-1H-imidazol-5-yl)methylene- 2 thiophenepropionic acid arginyl charge-neutralization-complex (I) is new: INDEPENDENT CLAIMS are also included for the following:compositions comprising (I) and a diuretic, calcium channel blocker,

beta -adrenoceptor blocker, renin inhibitor or angiotensin converting enzyme inhibitor; and (2) compositions comprising eprosartan or its methanesulphonate salt, a charge neutralization-complexing agent and a carrier.

USE - (I) is an angiotensin II blocker and is useful for treating hypertension, congestive heart failure and renal failure (claimed), also left ventricular hypertrophy regression, diabetic nephropathy, diabetic retinopathy, macular degeneration, haemorrhagic stroke, and for primary and secondary prevention of infarction, prevention of atheroma progression and the regression of atheroma, prevention of restenosis after angioplasty or bypass surgery, improving cognitive function, angina, glaucoma and CNS disorders (e.g. anxiety).

ADVANTAGE - (I) has increased lipophilicity, better dissolution profile and increased in vitro permeability through rabbit colon, compared with eprosartan monomethanesulphonate salt (EM). In an in-vitro dissolution study using granules of (I) and granules of EM, results for % eprosartan dissolved after 45, 120 and 225 minutes respectively were 32.81, 36.24 and 100.63% for (I), compared with 17.77, 19.64 and 58.52% for EM.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 51. Document ID: JP 01045348 A

L10: Entry 51 of 52 File: DWPI Feb 17, 1989

DERWENT-ACC-NO: 1989-097121
DERWENT-WEEK: 198913

TITLE: N-substd.-l-aminoacid derivs. prodn. - useful as intermediates for angiotensin converting enzyme inhibitors, by reacting 2-oxo-phenyl butyric acid(s) with l-aminoacid

PRIORITY-DATA: 1987JP-0200866 (August 13, 1987)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
JP 01045348 A	February 17, 1989		005	

INT-CL (IPC): C07 B 53/00; C07 C 99/00; C07 C 101/12

ABSTRACTED-PUB-NO: JP 01045348A
BASIC-ABSTRACT:

N-Substd.-L-amino acid derivatives (I) are produced by reacting a 2-oxo-4-phenylacetic acid deriv. (II) with an L-amino acid deriv. (III) in the presence of a catechol borane (IV). (R4 = H, alkyl or alkyloxy) (R1 and R3 are each or carboxy-protecting group; R2 = lower alkyl). Pref. the reaction is in solvent in the presence of (IV) at -78 deg.C to room temperature,pref. at -20 deg.C to 0 deg.C..

USE/ADVANTAGE - (I) are useful as an intermediate for angiotensin converting enzyme inhibitors. The process gives (I) selectively.

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 52. Document ID: DD 225131 A

L10: Entry 52 of 52 File: DWPI Jul 24, 1985

DERWENT-ACC-NO: 1985-276844
DERWENT-WEEK: 198545

TITLE: Prodn. of hypotensive 3,4-di:hydro-quinazolin-4-one derivs. - from 3-amino-3,4-di:hydro-quinazolin-4-one derivs.

INVENTOR: HEDER, G; KNOKE, D ; KOTTKE, K ; KUHMSTEDT, H ; SIEMS, W E ; WEHLAN, H

PRIORITY-DATA: 1984DD-0259720 (January 30, 1984)

PATENT-FAMILY:

PUB-NO	PUB-DATE	LANGUAGE	PAGES	MAIN-IPC
DD 225131 A	July 24, 1985		014	

INT-CL (IPC): C07 D 293/95

ABSTRACTED-PUB-NO: DD 225131A
BASIC-ABSTRACT:

Prodn. of 2-substd. 3,4-dihydroquinazolin -4-ones (I) is effected by deamination of 2-substd. 3-amino-3,4 -dihydroquinazolin-4-ones (II).

Cpds. of formula (Ia) are prepd. by reducing cpds. (IIa) with HNO2: R1 = NHAr; R2 = H or halogen; Ar = phenyl opt. substd. by Cl or Br.

USE - (I) are hypotensives acting by inhibition of angiotensin-converting enzyme (IC50 = 2-200 micromole/l). They are also stated to be useful as antihistamines and analgesics.

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Search Results - Record(s) 1 through 20 of 20 returned.

☐ 1. Document ID: US 20050282154 A1

Using default format because multiple data bases are involved.

L11: Entry 1 of 20 File: PGPB Dec 22, 2005

PGPUB-DOCUMENT-NUMBER: 20050282154
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20050282154 A1

TITLE: Angiotensin-converting enzyme-2 as a receptor for the SARS coronavirus

PUBLICATION-DATE: December 22, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Farzan, Michael R.	Cambridge	MA	US
Li, Wenhui	Boston	MA	US
Moore, Michael J.	Cambridge	MA	US

US-CL-CURRENT: 435/5; 435/235.1, 435/456

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 2. Document ID: US 20050249780 A1

L11: Entry 2 of 20 File: PGPB Nov 10, 2005

PGPUB-DOCUMENT-NUMBER: 20050249780
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20050249780 A1

TITLE: Functional foods and process for producing functional food

PUBLICATION-DATE: November 10, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Suzuki, Masayuki	Kanagawa		JP
Tonouchi, Hidekazu	Kanagawa		JP
Yoshioka, Norimichi	Kanagawa		JP
Uchida, Masayuki	Kanagawa		JP
Oda, Munehiro	Kanagawa		JP

US-CL-CURRENT: 424/439; 426/36

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 3. Document ID: US 20050249779 A1

L11: Entry 3 of 20 File: PGPB Nov 10, 2005

PGPUB-DOCUMENT-NUMBER: 20050249779
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20050249779 A1

TITLE: Processed cheese products and process for producing processed cheese

PUBLICATION-DATE: November 10, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Oda, Munehiro	Kanagawa		JP
Aizawa, Sigeru	Kanagawa		JP
Uchida, Masayuki	Kanagawa		JP
Suzuki, Masayuki	Kanagawa		JP
Sase, Manabu	Kanagawa		JP

US-CL-CURRENT: 424/439; 426/36

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 4. Document ID: US 20050203168 A1

L11: Entry 4 of 20 File: PGPB Sep 15, 2005

PGPUB-DOCUMENT-NUMBER: 20050203168
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20050203168 A1

TITLE: Angiotensin converting enzyme inhibitor use for treatment and prevention of gastrointestinal disorders

PUBLICATION-DATE: September 15, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Teitelbaum, Daniel H.	Ann Arbor	MI	US
Wildhaber, Barbara E.	Geneva		CH

US-CL-CURRENT: 514/423

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 5. Document ID: US 20050147600 A1

L11: Entry 5 of 20 File: PGPB Jul 7, 2005

PGPUB-DOCUMENT-NUMBER: 20050147600
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20050147600 A1

TITLE: Angiotensin converting enzyme homolog and uses therefor

PUBLICATION-DATE: July 7, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Acton, Susan	Lexington	MA	US
Robison, Keith E.	Wilmington	MA	US
Hsieh, Frank Y.	Lexington	MA	US

US-CL-CURRENT: 424/94.64; 435/226, 435/320.1, 435/325, 435/6, 435/69.1, 435/7.92, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

☐ 6. Document ID: US 20050113298 A1

L11: Entry 6 of 20 File: PGPB May 26, 2005

PGPUB-DOCUMENT-NUMBER: 20050113298
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20050113298 A1

TITLE: Receptor binding peptides derived from the SARS S protein

PUBLICATION-DATE: May 26, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Farzan, Michael R.	Cambridge	MA	US
Li, Wenhui	Boston	MA	US

US-CL-CURRENT: 514/12; 435/320.1, 435/325, 435/69.1, 530/350, 530/388.26, 536/23.5

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 7. Document ID: US 20040265882 A1

L11: Entry 7 of 20 File: PGPB Dec 30, 2004

PGPUB-DOCUMENT-NUMBER: 20040265882
PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20040265882 A1

TITLE: Diabetes gene

PUBLICATION-DATE: December 30, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
McGrail, Maura	Salt Lake City	UT	US
Russell, Deanna L.	Salt Lake City	UT	US
Shattuck, Donna M.	Salt Lake City	UT	US

US-CL-CURRENT: 435/6; 435/320.1, 435/325, 435/69.4, 530/303, 536/23.5

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 8. Document ID: US 20040241774 A1

L11: Entry 8 of 20 File: PGPB Dec 2, 2004

PGPUB-DOCUMENT-NUMBER: 20040241774
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040241774 A1

TITLE: Kits for diagnosing kidney diseases

PUBLICATION-DATE: December 2, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Kazuo, Uchida	Kyoto		JP

US-CL-CURRENT: 435/7.92

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 9. Document ID: US 20040229219 A1

L11: Entry 9 of 20 File: PGPB Nov 18, 2004

PGPUB-DOCUMENT-NUMBER: 20040229219
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040229219 A1

TITLE: Method of inhibiting human metapneumovirus and human coronavirus in the prevention and treatment of severe acute respiratory syndrome (SARS)

PUBLICATION-DATE: November 18, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Gallaher, William R.	Pearl River	LA	US
Garry, Robert F.	New Orleans	LA	US

US-CL-CURRENT: 435/5; 530/395

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 10. Document ID: US 20040121429 A9

L11: Entry 10 of 20 File: PGPB Jun 24, 2004

PGPUB-DOCUMENT-NUMBER: 20040121429
PGPUB-FILING-TYPE: corrected
DOCUMENT-IDENTIFIER: US 20040121429 A9

TITLE: Methods and compositions for modulating ACE-2 activity

PUBLICATION-DATE: June 24, 2004

PRIOR-PUBLICATION:

DOC-ID	DATE
US 0138894 A1	July 24, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Parry, Tom J.	Walkersville	MD	US
Sekut, Les	Ijamsville	MD	US
Rosen, Craig A.	Laytonsville	MD	US
Albert, Vivian R.	Rockville	MD	US
Sanyal, Indrajit	Bethesda	MD	US
Huang, Lili	Burlington	MA	US
Wescott, Charles R.	Belmont	MA	US

US-CL-CURRENT: 435/69.1; 435/226, 435/320.1, 435/325, 514/12, 530/324

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 11. Document ID: US 20040082496 A1

L11: Entry 11 of 20 File: PGPB Apr 29, 2004

PGPUB-DOCUMENT-NUMBER: 20040082496
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040082496 A1

TITLE: ACE-2 modulating compounds and methods of use thereof

PUBLICATION-DATE: April 29, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Acton, Susan L.	Lexington	MA	US
Ocain, Timothy D.	Framingham	MA	US
Gould, Alexandra E.	Cambridge	MA	US
Dales, Natalie A.	Arlington	MA	US
Guan, Bing	Brighton	MA	US
Brown, James A.	Framingham	MA	US
Patane, Michael	Andover	MA	US
Kadambi, Vivek J.	Boxboro	MA	US
Solomon, Michael	Medford	MA	US
Stricker-Krongrad, Alain	Lexington	MA	US

US-CL-CURRENT: 514/1; 424/146.1

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw De

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☐ 12. Document ID: US 20040033582 A1

L11: Entry 12 of 20 File: PGPB Feb 19, 2004

PGPUB-DOCUMENT-NUMBER: 20040033582
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040033582 A1

TITLE: Human single nucleotide polymorphisms

PUBLICATION-DATE: February 19, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Edmonds, Manling-Ma	Lawrenceville	PA	US
Hui, Lester	Fairfax	VA	US
Perrone, Mark	Boston	MA	US
Powell, James R.	Lumberville	PA	US
Ramanathan, Chandra S.	Wallingford	CT	US
Swanson, Brian	Yardley	PA	US
Tsuchihashi, Zenta	Skillman	NJ	US
Zerba, Kim	New Hope	PA	US

US-CL-CURRENT: 435/226; 435/320.1, 435/325, 435/6, 435/69.1, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw De

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☐ 13. Document ID: US 20030203834 A1

L11: Entry 13 of 20 File: PGPB Oct 30, 2003

PGPUB-DOCUMENT-NUMBER: 20030203834

PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030203834 A1

TITLE: Angiotensin-(1-7) and angiotensin-(1-7) agonists for inhibition of cancer cell growth

PUBLICATION-DATE: October 30, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Tallant, E. Ann	Lewisville	NC	US
Gallagher, Patricia E.	Lewisville	NC	US
Ferrario, Carlos M.	Winston-Salem	NC	US

US-CL-CURRENT: 514/1; 514/12, 514/573

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 14. Document ID: US 20030138894 A1

L11: Entry 14 of 20 File: PGPB Jul 24, 2003

PGPUB-DOCUMENT-NUMBER: 20030138894
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030138894 A1

TITLE: Methods and compositions for modulating ACE-2 activity

PUBLICATION-DATE: July 24, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Parry, Tom J.	Walkersville	MD	US
Sekut, Les	Ijamsville	MD	US
Rosen, Craig A.	Laytonsville	MD	US
Albert, Vivian R.	Rockville	MD	US
Sanyal, Indrajit	Bethesda	MD	US
Huang, Lili	Burlington	MA	US
Wescott, Charles R.	Belmont	MA	US

US-CL-CURRENT: 435/69.1; 435/226, 435/320.1, 435/325, 514/12, 530/324

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 15. Document ID: US 20030113726 A1

L11: Entry 15 of 20 File: PGPB Jun 19, 2003

PGPUB-DOCUMENT-NUMBER: 20030113726
PGPUB-FILING-TYPE: new

DOCUMENT-IDENTIFIER: US 20030113726 A1

TITLE: Human single nucleotide polymorphisms

PUBLICATION-DATE: June 19, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Tsuchihashi, Zenta	Pennington	NJ	US
Hui, Lester	Fairfax	VA	US
Zerba, Kim	New Hope	PA	US
Ma-Edmonds, Manling	Lawrenceville	NJ	US
Perrone, Mark	Princeton	NJ	US
Swanson, Brian	Yardley	PA	US
Powell, James	Lumberville	PA	US

US-CL-CURRENT: 435/6; 435/226, 435/320.1, 435/325, 435/69.1, 536/23.2

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 16. Document ID: US 20030091557 A1

L11: Entry 16 of 20 File: PGPB May 15, 2003

PGPUB-DOCUMENT-NUMBER: 20030091557
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030091557 A1

TITLE: Methods and compositions for modulating ACE-2 activity

PUBLICATION-DATE: May 15, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Parry, Tom J.	Walkersville	MD	US
Sekut, Les	Ijamsville	MD	US

US-CL-CURRENT: 424/94.64

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 17. Document ID: US 20030086920 A1

L11: Entry 17 of 20 File: PGPB May 8, 2003

PGPUB-DOCUMENT-NUMBER: 20030086920
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030086920 A1

TITLE: Use of des-Aspartate-angiotensin I as an agent for the treatment and

prevention of glomerulosclerosis and renal failure

PUBLICATION-DATE: May 8, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Sim, Meng Kwoon	Singapore		SG
Tan, Chorh Chuan	Singapore		SG

US-CL-CURRENT: 424/94.64

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw D

☐ 18. Document ID: US 20030055086 A1

L11: Entry 18 of 20 File: PGPB Mar 20, 2003

PGPUB-DOCUMENT-NUMBER: 20030055086
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030055086 A1

TITLE: Amino acid derivatives and use thereof as nep, ace and ece inhibitors

PUBLICATION-DATE: March 20, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Roques, Bernard P.	Cabanis		FR
Fournie-Zaluski, Marie-Claude	Paris		FR
Inguimbert, Nicolas	Cachan		FR
Poras, Herve	Alfortville		FR
Scalbert, Elizabeth	Paris		FR
Bennejean, Caroline	Charenton Le Pont		FR
Renard, Pierre	Le Chesnay		FR

US-CL-CURRENT: 514/336; 514/151, 514/397, 514/400, 514/414, 514/419, 546/264, 546/323, 548/312.7, 548/339.1, 548/455, 548/496

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw D

☐ 19. Document ID: US 20030036208 A1

L11: Entry 19 of 20 File: PGPB Feb 20, 2003

PGPUB-DOCUMENT-NUMBER: 20030036208
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030036208 A1

TITLE: Drug screening and diagnosis based on paracrine tubular renin-angiotensin system

PUBLICATION-DATE: February 20, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Rohrwasser, Andreas	Salt Lake City	UT	US
Morgan, Terry	Salt Lake City	UT	US
Lalouel, Jean-Marc	Salt Lake City	UT	US

US-CL-CURRENT: 436/536

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 20. Document ID: US 20030017989 A1

L11: Entry 20 of 20 File: PGPB Jan 23, 2003

PGPUB-DOCUMENT-NUMBER: 20030017989
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20030017989 A1

TITLE: Use of angiotensin I derivative as an agent for the treatment and prevention of infarction-related cardiac injuries and disorders

PUBLICATION-DATE: January 23, 2003

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Sim, Meng Kwoon	Singapore		SG

US-CL-CURRENT: 514/15

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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Clear | Generate Collection | Print | Fwd Refs | Bkwd Refs | Generate OACS

Terms	Documents
angiotensin adj3 converting enzyme adj3 related carboxypeptidse or angiotensin adj3 converting enzyme adj3 2	20

Display Format: - Change Format

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Hit List

First Hit | Clear | Generate Collection | Print | Fwd Refs | Bkwd Refs | Generate OACS

Search Results - Record(s) 1 through 5 of 5 returned.

☐ 1. Document ID: US 3282694 A

Using default format because multiple data bases are involved.

L3: Entry 1 of 5 File: USOC Nov 1, 1966

US-PAT-NO: 3282694
DOCUMENT-IDENTIFIER: US 3282694 A

TITLE: N-substituted aminoalkyl mercaptan metal salt fixing agents

DATE-ISSUED: November 1, 1966

INVENTOR-NAME: LUCKEY GEORGE W

US-CL-CURRENT: 430/404; 430/428, 430/429, 430/453, 430/966

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Ds

☐ 2. Document ID: US 3134640 A

L3: Entry 2 of 5 File: USOC May 26, 1964

US-PAT-NO: 3134640
DOCUMENT-IDENTIFIER: US 3134640 A

TITLE: Preparation of chromium oxychloride, crocl

DATE-ISSUED: May 26, 1964

INVENTOR-NAME: HENGEVELD FRANK W; KIRMAN TAYLOR

US-CL-CURRENT: 423/472, 526/169, 526/348, 526/351, 526/352

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw Ds

☐ 3. Document ID: US 2648013 A

L3: Entry 3 of 5 File: USOC Aug 4, 1953

US-PAT-NO: 2648013
DOCUMENT-IDENTIFIER: US 2648013 A

TITLE: Fluorescent screen

DATE-ISSUED: August 4, 1953

INVENTOR-NAME: STERRETT SMITH JAMES

US-CL-CURRENT: 250/488.1; 156/246, 156/67, 264/21, 264/255, 976/DIG.439

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 4. Document ID: US 2590139 A

L3: Entry 4 of 5 File: USOC Mar 25, 1952

US-PAT-NO: 2590139
DOCUMENT-IDENTIFIER: US 2590139 A

TITLE: Process for preparing crystalline streptomycin hydrochloride

DATE-ISSUED: March 25, 1952

INVENTOR-NAME: WOLF FRANK J

US-CL-CURRENT: 536/16

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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☐ 5. Document ID: US 2472715 A

L3: Entry 5 of 5 File: USOC Jun 7, 1949

US-PAT-NO: 2472715
DOCUMENT-IDENTIFIER: US 2472715 A

TITLE: Piezoelectric crystal apparatus

DATE-ISSUED: June 7, 1949

INVENTOR-NAME: MASON WARREN P

US-CL-CURRENT: 310/360; 310/368

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw De

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Clear | Generate Collection | Print | Fwd Refs | Bkwd Refs | Generate OACS

Terms	Documents
(angiotensin adj3 converting enzyme adj3	

related carboxypeptidse or angiotensin adj3 converting enzyme adj3 2 or ACE adj3 2) same crystal and x-ray	5

Display Format: - Change Format

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Search Results - Record(s) 1 through 3 of 3 returned.

☐ 1. Document ID: US 20050070599 A1

Using default format because multiple data bases are involved.

L4: Entry 1 of 3 File: PGPB Mar 31, 2005

PGPUB-DOCUMENT-NUMBER: 20050070599
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20050070599 A1

TITLE: Crystal forms of 4-[4-(4-fluorophenoxy)benzenesulfonylamino]-tetrahydropyr-an-4-carboxylic acid hydroxyamide

PUBLICATION-DATE: March 31, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Ewing, Marcus Douglas	Colchester	CT	US
Li, Zheng Jane	Quaker Hill	CT	US
Reiter, Lawrence Alan	Mystic	CT	US
Tickner, Derek Lawrence	Waterford	CT	US

US-CL-CURRENT: 514/459; 549/424

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw De

☐ 2. Document ID: US 20050070579 A1

L4: Entry 2 of 3 File: PGPB Mar 31, 2005

PGPUB-DOCUMENT-NUMBER: 20050070579
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20050070579 A1

TITLE: Crystals of taxane derivative and process for their production

PUBLICATION-DATE: March 31, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Uchida, Seishiro	Tokyo		JP
Takayanagi, Yoshihiro	Tokyo		JP
Ono, Makoto	Tokyo		JP

US-CL-CURRENT: 514/337; 546/281.7

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

☐ 3. Document ID: US 20050032183 A1

L4: Entry 3 of 3 File: PGPB Feb 10, 2005

PGPUB-DOCUMENT-NUMBER: 20050032183
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20050032183 A1

TITLE: Crystalline polypeptides

PUBLICATION-DATE: February 10, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Osslund, Timothy D.	Camarillo	CA	US
Clogston, Christi L.	Newbury Park	CA	US
Crampton, Shon Lee	Los Angeles	CA	US
Bass, Randal B.	Seattle	WA	US

US-CL-CURRENT: 435/183; 530/350, 702/19

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWIC | Draw D

Clear | Generate Collection | Print | Fwd Refs | Bkwd Refs | Generate OACS

Terms	Documents
(angiotensin adj3 converting enzyme adj3 related carboxypeptidse or angiotensin adj3 converting enzyme adj3 2 or ACE adj3 2) same crystal and x-ray	3

Display Format: - Change Format

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Hit List

First Hit | Clear | Generate Collection | Print | Fwd Refs | Bkwd Refs | Generate OACS

Search Results - Record(s) 1 through 4 of 4 returned.

☐ 1. Document ID: US 20060024298 A1

L7: Entry 1 of 4 File: PGPB Feb 2, 2006

PGPUB-DOCUMENT-NUMBER: 20060024298
PGPUB-FILING-TYPE:
DOCUMENT-IDENTIFIER: US 20060024298 A1

TITLE: Optimized Fc variants

PUBLICATION-DATE: February 2, 2006

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Lazar; Gregory Alan	Los Angeles	CA	US
Dang; Wei	Pasadena	CA	US
Desjarlais; John J.	Pasadena	CA	US
Karki; Sher Bahadur	Pasadena	CA	US
Vafa; Omid	Monrovia	CA	US
Hayes; Robert	Paoli	PA	US

US-CL-CURRENT: 424/133.1; 530/387.3

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw Ds

☐ 2. Document ID: US 20050032183 A1

L7: Entry 2 of 4 File: PGPB Feb 10, 2005

PGPUB-DOCUMENT-NUMBER: 20050032183
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20050032183 A1

TITLE: Crystalline polypeptides

PUBLICATION-DATE: February 10, 2005

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Osslund, Timothy D.	Camarillo	CA	US
Clogston, Christi L.	Newbury Park	CA	US
Crampton, Shon Lee	Los Angeles	CA	US

Bass, Randal B. Seattle WA US

US-CL-CURRENT: 435/183; 530/350, 702/19

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw D

☐ 3. Document ID: US 20040033532 A1

L7: Entry 3 of 4 File: PGPB Feb 19, 2004

PGPUB-DOCUMENT-NUMBER: 20040033532
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20040033532 A1

TITLE: Use of three-dimensional crystal structure coordinates to design and synthesize domain-selective inhibitors for angiotensin-converting enzyme (ACE)

PUBLICATION-DATE: February 19, 2004

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Ehlers, Mario R. W.	Mercer Island	WA	US
Holmquist, Barton	Eagle	NE	US

US-CL-CURRENT: 435/7.1; 702/19

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw D

☐ 4. Document ID: US 20020197628 A1

L7: Entry 4 of 4 File: PGPB Dec 26, 2002

PGPUB-DOCUMENT-NUMBER: 20020197628
PGPUB-FILING-TYPE: new
DOCUMENT-IDENTIFIER: US 20020197628 A1

TITLE: Screening methods for identifying ligands

PUBLICATION-DATE: December 26, 2002

INVENTOR-INFORMATION:

NAME	CITY	STATE	COUNTRY
Stewart, Lansing J.	Bainbridge Island	WA	US

US-CL-CURRENT: 435/6; 435/7.1, 702/19

Full | Title | Citation | Front | Review | Classification | Date | Reference | Sequences | Attachments | Claims | KWMC | Draw D

Clear | Generate Collection | Print | Fwd Refs | Bkwd Refs | Generate OACS